The Journal of Pediatrics

VOL. 15 OCTOBER, 1939 NO. 4

Original Communications

NITROGEN METABOLISM DURING THE ORAL AND PARENTERAL ADMINISTRATION OF THE AMINO ACIDS OF HYDROLYZED CASEIN

ALFRED T. SHOHL, M.D., ALLAN M. BUTLER, M.D., KENNETH D. BLACKFAN, M.D., AND ELSIE MACLACHLAN
BOSTON, MASS.

THE researches of Osborne and Mendel, and more recently of Rose (1938) and his co-workers, have greatly advanced the science of nutrition with regard to the proteins and amino acids essential for adequate nutrition of experimental animals. A search of the literature has revealed no report on the feeding to human beings of amino acids as the sole source of nitrogen. Osborne and Mendel (1916) showed that casein at a level of 8 to 18 per cent of the dry diet provides adequate protein intake for rats. The purpose of this study was to test whether the amino acids supplied by this protein were adequate for nutrition so far as this can be determined by nitrogen balance measurements over short periods of observation. The balance studies were carried out on infants during (1) oral administration and (2) intravenous administration of the amino acids of casein.

Hydrolyzates of protein may be prepared by either enzymatic or acid cleavage. The product used in this study was an enzymatic hydrolyzate of casein prepared by Mead Johnson and Co. This contains, according to our measurement, 11.9 per cent of nitrogen, of which over 60 per cent is present as amino acids. No protein is present, as shown by chemical tests. The absence of native casein has also been shown by negative sensitization tests with guinea pigs.*

PART I. ORAL ADMINISTRATION

The food used for oral administration was prepared by Mead Johnson and Co. Its composition is given in Table I. This preparation was

From the Department of Pediatrics, Harvard Medical School, and the Infants' Hospital and the Children's Hospital.

Assisted by a grant from Mead Johnson and Co.

Presented before the American Pediatric Society, Skytop, Pa., April, 1939.

*Dr. P. S. Prickett of the Mead Johnson Research Laboratory, personal communication.

TABLE I

COMPOSITION OF AMINO ACID FOOD

	AMINO ACID FOOD POWDER			DILUTED FEEDING*	MILK FEEDING*	
	PER CENT	CAL./GM.	PER CENT OF CAL.	PER CENT		PER CENT
Amino acids	20	0.8	17	2.7	Protein	2.3
Olive oil	18	1.6	36	2.4	Milk fat	2.6
Carbohydrate	56	2.3	47	7.5	Carbohydrate	8.3
Minerals	5					
Total		4.7				

*In these two columns are given the composition of a feeding consisting of 13.5 gm. of amino acid food diluted to 100 c.c. with water and a modified milk feeding consisting of 2/3 milk, 1/3 water, and 5 per cent added sugar.

in powder form. Water was added and the mixture boiled for 5 minutes. The resultant smooth emulsion did not separate in 24 hours. It has a rather strong yeasty taste but was taken well by the infants. Each subject was given 5 feedings per day. The total daily intake constituted about 50 Cal. per pound of body weight (110 Cal./kg.), 2.5 oz. of fluid per pound (165 c.c./kg.), 2 gm. of amino acids per pound (4.4 gm./kg.), or 0.52 gm. of N/kg. This food was supplemented with 5 drops of percomorph oil (7500 units of vitamin A and 1000 units of vitamin D), 0.345 mg. of thiamin chloride, 10 mg. of nicotinic acid, and 25 mg. of cevitamic acid, per child per day.

For the control periods the same babies were given a mixture of evaporated milk, water, and karo syrup, so that the fluid, caloric, and nitrogen intakes were approximately the same as in the experimental periods. Vitamins A, C, and D only were given as supplements.

The patients were white, male, well babies, who were admitted to the hospital from institutions for the purposes of this study, with the following exceptions. One baby (S.) had congenital laryngeal stridor, one (W. McC.) had a low-grade upper respiratory infection throughout the period of the study, and one (B.) was brought to the hospital in an emaciated and dehydrated condition due to inadequate diet. The infants' weights varied from 3 to 7 kg., and their ages, from 2 to 7 months.

The infants were given the food for a preliminary period of 5 to 7 days before collections of urine and feces were begun. Occasionally a small amount of food was refused. This was analyzed for total nitrogen and the amount subtracted from the total offered. In two instances a small amount of food was regurgitated with a gas bubble immediately after feeding. This was so small in amount that no appreciable error ensued from estimating the amount thus lost. This was also subtracted from that offered and the net intake calculated.

The feces, in the majority of cases when the babies were fed amino acid food, were semiformed, slightly greenish, and small in amount. There were usually two or three movements per day. One baby was

TABLE II

DAILY NITROGEN METABOLISM DURING FEEDING OF MILK FORMULA (M), AMINO ACID FOOD (A), AND INTRAVENOUS ADMINISTRATION OF AMINO ACID SOLUTION WITH GLUCOSE AND NaCl (I)

SUBJECT	FOOD	DATE	WEIGHT (KG.)	NITROGEN INTAKE (GM.)	FECES	URINE						
					TOTAL N (GM.)	VOL. (C.C.)	pH	CREATININE (MG.)	UREA N (GM.)	NH_4 N (MG.)	NH_2 N (MG.)	TOTAL N (GM.)
A.	I	12/26-12/27/38	20	3.60	0.03	220	5.3	-	-	-	215	2.67
L.McC.	M	11/23-11/26/38	6.8-7.0	5.00	0.40	584	6.0	95	3.18	113	75	3.55
	M	11/28-12/ 1/38	7.0-7.2	5.00	0.47	507	6.1	103	2.93	124	90	3.38
	A	12/27-12/31/38	7.8	4.20	0.31	408	5.9	89	2.09	114	94	2.90
	A	1/23- 1/26/38	8.9-9.0	4.56	0.34	338	5.9	92	2.62	90	110	3.01
W.	I	1/ 2- 1/ 3/39	4.0	3.00	0.19	298	5.6	54	1.17	93	156	2.07
	M	1/18- 1/21/39	4.1-4.2	2.84	0.30	238	6.3	56	1.21	89	53	1.51
	A	1/30- 2/ 3/39	4.4	2.15	0.19	201	6.7	51	1.25	81	37	1.42
	I	2/ 7- 2/ 8/39	4.4	2.68	-	515	6.9	38	1.84	157	190	2.59
	A	2/13- 2/17/39	4.4	2.40	0.19	316	6.8	53	1.48	98	81	1.75
S.	M	1/30- 2/ 3/39	4.3	1.82	0.20	254	5.8	52	0.65	49	30	0.80
	A	2/ 6- 2/11/39	4.4	2.00	0.19	280	5.6	52	0.88	57	72	1.06
	A	2/13- 2/17/39	4.5	2.06	0.12	277	6.0	53	0.94	53	37	1.12
	I	3/ 6- 3/ 7/39	4.6	2.75	-	458	5.7	69	1.21	121	119	1.85
	M	3/14- 3/17/39	4.8-4.9	2.26	0.13	316	5.3	57	0.86	56	55	1.02
B.	A	2/13- 2/17/39	3.1-3.2	1.69	0.11	291	5.2	35	0.56	40	57	0.69
	A	2/27- 3/ 3/39	3.2-3.3	1.79	0.15	256	6.2	38	0.61	46	47	0.80
	I	3/ 6- 3/ 7/39	3.2	2.73	-	368	5.6	47	0.96	80	139	1.46
M.	M	3/ 6- 3/10/39	7.2-7.3	4.00	0.52	318	5.2	91	2.67	106	133	2.99
	A	3/13- 3/17/39	7.3-7.6	4.09	0.43	465	5.3	88	2.02	94	135	2.56
W.McC.	M	3/13- 3/17/39	5.8-6.0	3.33	0.32	337	5.4	78	1.97	99	77	2.22
	A	4/ 1- 4/ 4/39	6.2-6.4	3.37	0.27	336	5.5	73	1.92	131	185	2.26
	I	4/17- 4/18/39	6.6	1.31	-	480	5.0	78	1.51	176	65	2.06

slightly constipated. The feces were collected for three-day periods and analyzed for total nitrogen. The urine was collected daily for four-day periods. The volume was measured, and the pH was determined colorimetrically. The following analyses were made: total nitrogen (by a micro-Kjeldahl method), urea (gasometrically) (Peters and Van Slyke, 1932), ammonium (Folin, 1934), amino acids (Folin, 1934), and creatinine (Folin, 1934). The analyses were made daily, and the values which were in close agreement were averaged for the period.

The data, which comprise determinations for seven control periods and ten amino acid food periods on six infants, are given in Table II. The data can be interpreted more easily if they are expressed in terms which permit comparison of each experimental period with the control period. This is accomplished by stating the various nitrogenous substances in per cent of the total nitrogen excretion, and by calculating the balances both as per cent of the amount ingested and per kilogram of body weight. Inasmuch as each infant served as his own control, the data on infants of different weights and on different nitrogen intakes may therefore be averaged. A direct comparison of the response to the different types of food is thus afforded. Such calculations are given in Table III. In this table the data on patient B. are omitted from calculation because this subject had no control period, although the data did not differ significantly from those of the other infants in the group.

TABLE III

AVERAGE DAILY NITROGEN METABOLISM WITH ORAL AMINO ACID AND MILK FEEDINGS

FEEDINGS	N INTAKE	N RETENTION	N RETENTION / INTAKE	FECES N	TOTAL EXCRETED N	URINE									
						CREATININE	AMMONIUM N	TOTAL URINE N	UREA N	TOTAL URINE N	DETERMINED N	TOTAL URINE N	AMINO N	TOTAL URINE N
	Gm.	Gm.	Gm./kg.	Per cent	Per cent	Mg./kg.	Per cent	Per cent	Per cent	Per cent	Per cent	Per cent	Per cent	Per cent
Milk formula	3.80	0.91	0.17	24	13.6	13.1	4.2	84	92	3.5				
Amino acid food	3.64	0.83	0.14	23	11.4	11.8	4.6	82	90	5.0				

Of the various substances in the urine which were determined, only the amino acid fraction was appreciably different in the two periods. The amino acid content of the urine was greater during the period of amino acid feeding than during the milk feedings. However, amino acids formed a very small fraction of the nitrogen in the urine, and the difference averaged only 1.5 per cent of the urinary nitrogen. (See Table II.) The amino acid excretion was not always greater during the experimental than during the control periods.

The values for the nitrogen balances, whether expressed as gross balances per kilogram of body weight, or as per cent of the intake,

were indistinguishable for the two types of food. The data are interpreted to mean that the amino acid food resulted in a type of nitrogen metabolism which is very similar to that obtained with usual milk mixtures. The nitrogen excreted in the feces was less than that of the infants who received milk feedings. The difference is statistically significant, but probably not physiologically significant.*

PART II. INTRAVENOUS ADMINISTRATION

Amino acids have been injected intravenously into various experimental animals. Elman and Weiner (1939) have reported that they gave intravenous ingestions of an HCl digest of casein to a score of patients, of which eight are described. A review of the pertinent literature is given in their article.

In the present study the enzymatic hydrolyzate of casein was prepared for intravenous use as follows: It was first dissolved in freshly distilled water; this solution was passed through a sterile Seitz filter, and glucose and NaCl solutions were added to bring the mixture to the desired concentration. The final solution contained 2.5 per cent of amino acids (except in two instances where concentrations of 1.5 and 5.8 per cent were used), 10 per cent of glucose, and 0.45 per cent of NaCl. The pH of this mixture was about 4.5. In some cases the amino acid solution was partially neutralized by adding 1.5 gm. of $NaHCO_3$ per liter. This raised the pH to about 5.6-5.9. No significant differences in the results of administration were observed with solutions of different pH.

The amino acid solution was first given intravenously to one girl patient (A.) with tuberculous meningitis. She was 6 years of age and weighed about 20 kg. During 24 hours she received 1200 c.c. of a solution containing 2.5 per cent of amino acids, glucose, and NaCl as described above. This totals 3.6 gm. of nitrogen, or about 2/3 gm. of amino acids per kilogram of body weight. The urine was collected by an indying catheter. Although the child had a fever of from 105 to 107° F., she was in positive nitrogen balance and retained 0.90 gm. of nitrogen. No reaction followed the administration of the amino acid solution. She died of the meningitis 48 hours after the metabolism study. At necropsy the diagnosis was confirmed, and there were no findings of significance which could not be adequately explained by the fatal disease.

Subsequently the amino acid solutions were given intravenously to the patients to whom the amino acid mixture had been administered orally. The freshly prepared solutions were given intravenously by gravity without isolating or tying off the veins.† The fluid was given at a rate of 50 c.c. per hour, or less, for approximately 24 hours. The urine and feces were collected, as previously. The feces were

*The advantage of such a food for babies who are allergic to cow's milk is being investigated by Dr. L. W. Hill.

†We are indebted to the staff of the Infants' Hospital and especially to Dr. R. A. Ross, for the administration of the solutions.

small in amount, often lacking. Nothing was given by mouth. At the end of the period of parenteral therapy, the urine and feces were collected for two one-day periods during which time the control diet was again given.

Intravenous administration of amino acid solution was attempted on eight occasions in addition to that mentioned above. There were six febrile reactions, three of which were sufficient to prevent continuation of the injection. The fever subsided in about an hour. One infant had a convulsion after the injection was completed, and one had twitching of one arm. A macular rash lasting several hours appeared over both knees in one case. The fact that febrile reactions were observed, which were lacking in the cases of Elman and Weiner (1939), cannot be attributed to the fact that comparatively large amounts were used in this study, because elevation of temperature was observed in most cases a few hours after the injection was begun. Other investigators (unpublished data) have obtained febrile reactions with the HCl hydrolyzate, as well as with the enzymatic digest.

Data are presented from five periods on four infants, three of whom were studied also on both milk mixtures and the amino acid food. The data for the individual experiments are included in Table II and the balances calculated in Table IV. The feces of these intravenously

TABLE IV

NITROGEN METABOLISM FOR TWENTY-FOUR HOURS WITH INTRAVENOUS INJECTION OF AMINO ACIDS

SUBJECT	WEIGHT (KG.)	INTAKE					N RETENTION		
		VOLUME (C.C.)	AMINO ACIDS			N (GM.)	GM.	PER CENT OF INTAKE	GM./KG.
			GM.	GM./KG.	CONCENTRATION, PER CENT				
A.	20.0	1200	30.5	1.5	2.5	3.60	0.90	25	0.045
W.	4.0	500	25.8	6.4	5.1	3.00	0.74	22	0.185
W.	4.4	900	22.5	5.6	2.5	2.67	0.09	3	0.020
S.	4.5	939	23.5	5.2	2.5	2.75	0.90	33	0.200
B.	3.3	935	23.4	7.1	2.5	2.73	1.27	46	0.390
W. McC.	6.5	750	11.2	1.7	1.5	1.31	-0.75		-0.115

nourished infants were lacking or so scanty that their accurate demarcation for the period of intravenous therapy was not possible. The data show that, on the average, the amount of ammonium excreted in the urine was the same as when the infants were fed milk diets or the amino acid food. The amino acid excretion was approximately twice that of the control period. The undetermined nitrogen was also about twice that of the control period. What constitutes this fraction is unknown, but the undetermined nitrogen was increased at the expense of urea, which was diminished.

The data show that satisfactory nitrogen balances resulted when the sole source of nourishment for a period of 24 hours was a solution con-

taining amino acids, glucose, and NaCl, given intravenously. The balances in the afterperiods showed that the nitrogen retained during intravenous administration was not lost subsequently (data not included). Subject W. McC. had a negative nitrogen balance in all probability because the intake was below his nitrogen requirement.

The amount of amino acids retained was variable. Apart from biologic variation, some of the factors which determine the nitrogen retention are the total calories, the amount of amino acids per kilogram of body weight, the concentration of the amino acids, and the rate of injection. For example, in the case of W., the intravenous injections of the solution gave quite different results for the two periods. The studies are, however, too few in number to justify an attempt at exact evaluation of these factors. In general it is clear that, although the amounts of nitrogen given intravenously were smaller than when food was given orally, the balances were as large or larger.

The data given above confirm the findings of Elman and Weiner (1939) that amino acid solutions may be given intravenously and serve as a utilizable source of nitrogen. The metabolism data on infants give an evaluation of the amounts of nitrogen retained, and the character and amounts of the components excreted in the urine. These are comparable to the values obtained with usual diets or amino acid food. However, the experience in this study suggests that intravenous alimentation cannot be regarded as practical for infants until the source of untoward reactions can be determined and eliminated.

SUMMARY

Hydrolyzed casein, consisting largely of amino acids, was given orally to infants as the sole source of nitrogen. The amino acids, in the presence of the non-nitrogenous dietary essentials, gave positive nitrogen balances in all cases.

It was also found that positive and sufficient nitrogen balances were obtained by the intravenous administration of hydrolyzed casein together with glucose and sodium chloride. In most instances, however, there were untoward reactions, most prominently a marked elevation of body temperature. Further study is obviously required to identify and remove the cause of the febrile reactions which in our experience have limited the clinical utility of this form of intravenous nutrition.

REFERENCES

1. Elman, R., and Weiner, D. O.: J. A. M. A. **112**: 796, 1939.
2. Folin, O.: Laboratory Manual of Biological Chemistry, 5th ed., New York and London, 1934, D. Appleton-Century Co., 368 pp.
3. Osborne, T. B., and Mendel, L. B.: J. Biol. Chem. **26**: 1, 1916.
4. Peters, J. P., and Van Slyke, D. D.: Quantitative Clinical Chemistry, Vol. II, Baltimore, 1932, The Williams and Wilkins Co., 957 pp.
5. Rose, W. C.: Physiol. Rev. **18**: 109, 1938.

CHRONIC STRIDOR IN INFANCY

JAMES E. BOWMAN, M.D., AND CHEVALIER L. JACKSON, M.D.
PHILADELPHIA, PA.

THERE is often considerable confusion concerning the cause of respiratory stridor in infants. The trouble usually revolves around the difficult problem of the thymus gland. We have attempted to clarify the subject a little with a review of the literature and a study of thirty cases of infants presenting this symptom.

The medical literature dealing with this phenomenon and its causes seems to have become prominent in 1883 with Lees'[1] description of autopsy findings of a child who presented it during life. He found an epiglottis which curled inwards more than normal and the arytenoepiglottidean folds thin and in close approximation. Nine years later John Thomson[2] concluded, after careful study of five cases, that the stridor was due to "a central functional disorder consisting in a slight disturbance of the coordination which takes place in ordinary breathing between the thoracic muscles on the one hand and those of the larynx on the other." Following these, a number of writers reported series of cases in which this symptom was prominent. Sir St. Clair Thomson[3] emphasized the importance of direct laryngoscopy in accurate diagnosis. This procedure showed that in a large number of cases stridor was due to congenital malformation of the epiglottis or vestibule of the larynx. The use of direct laryngoscopy has also been fully discussed by Chevalier Jackson.[4] The excellent papers of Hill[5] and Kennedy and New,[6] Bagg,[7] Erreeart and Becco[8] should be mentioned among recent contributions.

Thirty case histories of infants seen consecutively to determine the cause of stridorous breathing form the basis for this paper. The patients were examined in the Chevalier Jackson Bronchoscopic Clinic and the Pediatric Department of the Temple University Hospital over a five-year period.

The objects of the work were several. First, it seemed desirable to develop a routine for examination which would lead to the most accurate diagnosis; second, we desired to determine the relative frequency of the more important causes of this interesting symptom in our patients; and last, we wished to ascertain the role of the thymus gland as a causative factor.

A complete examination of these infants was made, including the usual clinical studies of history, physical examination, and routine laboratory tests. A careful x-ray examination of the respiratory tract was carried out in all cases. Undoubtedly, the most important part of the study was the direct examination by the laryngoscope and the bronchoscope.

CAUSES OF STRIDOR

Fourteen, or nearly one-half, of the thirty infants were found to have supraglottic obstruction to inspiration due to deformity or flaccidity of the epiglottis, arytenoids, and/or aryepiglottic folds (Table I). This condition has been termed "congenital laryngeal stridor," "congenital relaxation of the larynx," and "congenital atony of the vocal cords." The designations, "exaggerated infantile type of larynx" and "laryngomalacio," attempt to describe as well as name the condition. In children who have this difficulty, the epiglottis and arytenoids, forming the upper rim of the larynx, are drawn over the entrance of this organ on inspiration to produce the stridor. Characteristically, in this group of our patients, the onset of the noisy breathing was at birth.

In five of our patients with noisy breathing there appeared to be pressure of an enlarged thymus gland on the trachea. Diagnosis in these depended a great deal on the finding, by the lateral x-ray, of kinking, narrowing, and displacement backward of the trachea by a shadow posterior to the manubrium of the sternum. More weight was given to any of these observations which were made during full inspiration. The classic work of Pancoast[9] is fundamental in the diagnosis and evaluation of thymic compression. Negative endoscopic examinations were reported in all of these cases. Before classifying a child in this group, definite improvement in the stridor before 48 hours after x-ray treatment was necessary. The onset of the symptom in this group was typically at the second or third month, and the stridor was more marked on expiration.

Ten per cent (three cases) of our patients were stridorous because of congenital malformations of the larynx other than those present in the first group. One had weblike ridges in the subglottic area; another had a thickening of one of the ventricular bands, and the third, a congenitally small larynx. In connection with this third case, it may be mentioned that important studies of the infant larynx, including measurements, were made by Gabriel Tucker,[10] and he states that "a subglottic measurement of 6 mm. or above may be considered normal in a well-developed infant; a measurement of 5 mm. is abnormally small, although not incompatible with life and development. A subglottic diameter of 4 mm., however, is to be considered an actual congenital stenosis when it is found in an otherwise normal infant."

Each of the eight remaining cases was given a different diagnosis: cyst of the thyroglossal duct with pressure of the tumor from the base of the tongue upon the larynx, tuberculosis of the bronchial lymph nodes, micrognathia, collapse of part of the trachea, possibly because of the congenitally deficient cartilaginous rings, congenital heart dis-

TABLE I

LIST OF THIRTY CASES DESCRIBED IN TEXT WITH SIGNIFICANT DATA

CASE	SYMPTOMS AND SIGNS				ENDOSCOPIC EXAMINATION	X-RAY EXAMINATION	DIAGNOSIS	ASSOCIATED CONDITIONS	REMARKS
	STRIDOR		CYANOSIS						
	PHASE OF RESPIRATION	AGE AT ONSET							
R. C.	Insp.	1 mo.	Yes	Marked indrawing of suprasternal notch. Harrison's groove	Epiglottis large and omega-shaped	Increased hilus markings	"Congenital laryngeal stridor"	Frequent upper respiratory infections	
W. W.	Insp.	Birth	No	Stridor in attacks, some indrawing. Harrison's groove	Epiglottis thickened, also aryepiglottic folds, with inspiratory pulling in	Right upper lobe. Atelectasis aet. 6 mo.	"Congenital laryngeal stridor." Chronic hypertrophic laryngitis	Ethmoiditis. Also right upper lobe atelectasis	
E. S.	Insp.	Birth	Occ.	Indrawing. Pigeon-breast	Epiglottis long and curved, draws over laryngeal aperture on inspiration	Enlarged thymus treated	"Congenital laryngeal stridor"		Some improvement after thymus treatment
J. M.	Insp.	Birth	No	Marked indrawing. Malnutrition due to excessive vomiting	Epiglottis showed some hypertrophic cystlike masses of tissue on postsurface. Epiglottis pulls in on inspiration	Enlarged thymus; no improvement after treatment	"Congenital laryngeal stridor"	Atelectasis at birth, cleared rapidly. Malnutrition	Aet. 6 mo. great improvement

TABLE I—CONT'D

B. N.	Insp.	Birth	No	Indrawing	Epiglottis and ary-epiglottic folds flabby, tend to pull in on inspiration	Normal	"Congenital laryngeal stridor"	None	
E. D.	Insp.	Birth	No	Indrawing. Malnutrition	Epiglottis soft, pulling over supralaryngeal opening on inspiration	Possible enlarged thymus	"Congenital laryngeal stridor"	Anemia and malnutrition. Diarrhea	Death. Autopsy: Infarcts of lung (hemorrhagic)
J. W.	Insp.	1st week	Spells	Overweight. Stridor in attacks. Some indrawing	Epiglottis pulls over on inspiration. Arytenoids thickened	Thymus treated. No improvement	"Congenital laryngeal stridor"	Diarrhea	Gradual improvement
W. H.	Insp.	3rd week	Yes	Circumaural cyanosis. Stridor in attacks	Epiglottis infantile type. Motility right vocal cord slightly impaired	Thymus treated. No improvement	"Congenital laryngeal stridor"		Gradual improvement
R. P.	Insp.	Birth	No	Some indrawing. Well nourished	Epiglottis flabby. Right arytenoid tends to overhang	Enlarged thymus with compression. No improvement with treatment	"Congenital laryngeal stridor"		No stridor aet. 2 yrs.
P. C.	Insp.	Birth	No	Slight indrawing	Epiglottis exaggerated infantile type. Asymmetrically curled	Enlarged thymus treated. No improvement	"Congenital laryngeal stridor"	Choking with feedings	

TABLE I—CONT'D

CASE	SYMPTOMS AND SIGNS				ENDOSCOPIC EXAMINATION	X-RAY EXAMINATION	DIAGNOSIS	ASSOCIATED CONDITIONS	REMARKS
	STRIDOR		CYANOSIS						
	PHASE OF RESPIRATION	AGE AT ONSET							
E. A.	Insp.	Birth	Yes	Marked indrawing	Flaccid superior laryngeal aperture	Enlarged thymus with compression. No improvement on treatment	"Congenital laryngeal stridor"	"Cold" caused marked increase in symptoms	Gradual improvement
C. A. R.	Insp.	Birth	No		Curled epiglottis	No	"Congenital laryngeal stridor"		
N. B.	Insp.	Birth	No		Epiglottis infantile omega type. Arytenoepiglottidean folds flabby and overhanging		"Congenital laryngeal stridor" persisting into adolescence		Some stridor aet. 11 yr. when endoscopy performed
D. W.	Insp.	Birth	Slight	Marked indrawing	Epiglottis omega. Edges curled	Thymus enlarged. No treatment	"Congenital laryngeal stridor"	Icterus gravis at birth. Poor development. Walked 2 yr.	Improved gradually
D. O. H.	Insp. and exp.	Birth		Indrawing	Epiglottis short and thickened; other tissues hypertrophic	Increase in soft tissues of larynx. Absence of laryngeal ventricle. Increase in hilar marks	Congenital laryngeal stenosis	Attacks of unconsciousness. Rickets	Improved following dilatation

TABLE I—CONT'D

J.O.B.	Insp. and exp.	Birth	No	Slight indrawing	Cords normal, series weblike ridges in anterior subglottic region. One-half narrowing of lumen	Subglottic swelling	Congenital subglottic web. Stenosis	Anemia and rickets	Was diagnosed enlarged thymus shortly after birth. Treated with no improvement. Tracheotomy required for relief of dyspnea. Decanulated after 2 yrs. Gradual improvement
E. G.	Insp.	Birth	No	Slight indrawing	Right arytenoid motionless. Right cord overhung by mass of right ventricular band	Some thymic enlargement. Not treated	Congenital malformation causing stenosis		
Mc. G.	Insp.	Birth	Yes	No indrawing	No tracheal compression	Thymus enlarged. No tracheal compression	Enlarged thymus gland	Good deal of vomiting	Stridor greatly improved after x-ray treatment
A.	Exp.	3 mo.	Slight	Scattered râles	None	Enlarged thymus. Tracheal compression	Enlarged thymus gland	None	Chest signs from congestion due to thymus
C. W.	Exp.	3 mo.	No	Asthmatoid wheeze at mouth. Crackling râles (scattered)	Bronchitis (purulent) at 4 mo.	Enlarged thymus (later bronchopneumonia). Treatment by x-ray with improvement	Enlarged thymus, purulent bronchitis (?), bronchopneumonia	Pulmonary condition complicated	Great improvement after x-ray treatment of thymus

TABLE I—CONT'D

CASE	SYMPTOMS AND SIGNS				ENDOSCOPIC EXAMINATION	X-RAY EXAMINATION	DIAGNOSIS	ASSOCIATED CONDITIONS	REMARKS
	STRIDOR		CYANOSIS						
	PHASE OF RESPIRATION	AGE AT ONSET							
J. B.	Insp. and some exp.	Birth	No	No	None	Thymus enlarged with tracheal compression. Stridor disappeared after x-ray treatment	Enlarged thymus gland	None	X-ray treatment cured stridor
W. W.	Insp.	3 wk.	No	No	None	Thymus enlarged with compression of trachea	Enlarged thymus gland	None	X-ray treatment caused marked improvement in stridor
W. H.	Insp.	1 mo.	?	Indrawing. Diffuse consolidation of lungs	None	Yes—did not find cause	Cyst of thyroglossal duct (at base of tongue)	Congenital syphilis	Death, hemorrhagic pneumonia
D. N.	Exp.	2 mo.	No	Right-sided consolidation. Asthmatoid wheeze	Yes. Pus in bronchial tubes	Right-sided pneumonia	Pulmonary tuberculosis (bronchial gland)	Tuberculous pneumonia	Death. Autopsy proved cause of stridor
R. G.	Insp.	Birth	Slight	Deformity of jaw	Normal findings	No abnormal findings	Micrognathia	Great deal of feeding difficulty. Cleft palate	

TABLE I—CONT'D

A. D. C.	Insp.	Birth	Spells	Indrawing		Exp. collapse of trachea	Collapse of trachea		Greatly improved aet. 5 mo.
K. S.	Insp.	Birth	Yes	Typical finding of tetralogy of Fallot	None attempted	Coeur-en-sabot	Congenital heart disease (pressure on trachea)		Death due to tetralogy of Fallot. Aorta from right and left ventricle
R. S.	Insp.	5 mo.	No	Athetoid movements. Underdeveloped physically and mentally. Carpopedal spasms. Normal blood calcium and phosphorus	None	No abnormal findings	Undetermined. Child evidently had birth injury or cerebral agenesis	Carpopedal spasm. Irregular movements of extremities. Physical and mental underdevelopment marked	Death. Autopsy did not reveal cause of death
J. O'B.	Mostly insp., some expir.	Birth	Slight	Many scattered moist râles	Arytenoids and posterior commissure thickened; cords normal except for mild chronic inflammation		Chronic hypertrophic laryngitis	Positive tuberculin. (No other signs of infection)	
N. S.	Insp. and expir.	Birth	No	Indrawing	Congestion of pharynx and larynx; epiglottis short and thickened; subglottic swelling	Inflammatory process in larynx and subglottic portion of trachea	Chronic hypertrophic laryngitis. "Congenital laryngeal stridor"	None	

ease, hypertrophic laryngitis, hypertrophic laryngitis associated with congenital laryngeal stridor. In one case, the cause of the altered breathing was not determined.

A careful study was made of the position of the enlarged thymus gland in our thirty patients. The requirements for a diagnosis of this as a cause of stridor have been given above.

All of our cases were examined by the roentgen ray for enlargement of the thymus gland. Twenty-one were reported as having some degree of enlargement, and nine, as normal. Only five of the enlarged gland group were definitely improved following x-ray therapy, while five others were temporarily benefited. In nine there was no change in the symptoms, and two were not treated. All of these facts reaffirm the difficulty in estimating the importance of this troublesome diagnosis in cases studied because of noisy breathing. We have learned that an endoscopic examination will often clear up questionable situations, and we recommend its inclusion in all studies of patients with stridor.

CONCLUSIONS

1. The causes of stridorous breathing in thirty consecutive infants chronically affected included fourteen children with congenital excessive curling and flaccidity of the epiglottis, five with enlarged thymus, and three with congenital malformations of the larynx other than excessive curling of the epiglottis or flaccidity.

2. Satisfactory study of a child with stridor should include the careful x-ray examination of the neck and chest in both planes and an endoscopic examination of the larynx and trachea.

REFERENCES

1. Lees, D. B.: Tr. Path. Soc. Lond. **34:** 19, 1883.
2. Thomson, J.: Edinburgh M. J. **38:** 205, 1892.
3. Thomson, St. Clair: Diseases of the Nose and Throat, London, 1926, D. Appleton-Century Co., p. 505.
4. Jackson, Chevalier: Peroral Endoscopy and Laryngeal Surgery, St. Louis, 1915, The Laryngoscope Company, p. 463; The Larynx and Its Diseases, Philadelphia, 1937, W. B. Saunders Co.
5. Hill, Frederick T.: Laryngoscope **40:** 44, 1930.
6. Kennedy, Roger L. J., and New, Gordon B.: J. A. M. A. **96:** 16, 1931.
7. Bagg, Claire: Monatschr. f. Kinderh. **45:** 102, 1929.
8. Errecart, P. L., and Becco, R. V.: An. de oto-rino-laring. d. Uruguay **4:** 5, 1934.
9. Pancoast, Henry K.: Am. J. M. Sc. **180:** 745, 1930.
10. Tucker, Gabriel: J. A. M. A. **99:** 1899, 1932.

SWIMMING BEHAVIOR OF THE HUMAN INFANT

MYRTLE B. MCGRAW, PH.D.
NEW YORK, N. Y.

THE swimming behavior of the human infant bears striking testimony to the phylogenesis of man. Literature on the subject is sparse, limited largely to comments on the random movements of the newborn infant having a swimminglike quality. The only instances of actual experimental evidence cited are those of Watson[1] and the writer.[2] Watson's observations were on the behavior of three infants tested immediately after birth, as soon as breathing had been well established. His method was to support the baby's back with his hands and gradually lower him in a supine position into the water, maintained at body temperature, so that the body was immersed, but the face was above the water level, thereby preventing water from entering the respiratory passages. Watson report, "Violent expression of fear—a cry, checking of breathing, followed by deeper inspiration and rapid, entirely uncoordinated, slashing of hands and feet were all that could be observed." On the basis of these observations Watson discounts any evidence of swimming movements in the newborn behavior repertoire.

The present report comprises a more intensive study of the data which formed the basis of the descriptive analysis reported in "Growth."[2] Descriptive notes and cinema records were accumulated on 42 different infants, ranging in age from 11 days to 2½ years. Observations of the same infants were repeated at different intervals, the total number of observations on the 42 babies being 445. Of this total, 164 consisted of motion picture records, and 281 were in the nature of written notes. The number of repeated observations on the same child varied from 2 to 51, the median being 10. Although in several cases these repeated observations extended over a period of 18 or 20 months, the data were insufficient to justify longitudinal analysis. On the other hand the fact that the same children were tested at different intervals over a period of time indicates, more convincingly than purely cross-sectional observations would, that the changes in this behavior pattern have developmental import.

At each examination the baby was placed in three different positions: (1) With the hands of the experimenter placed under his chin and on the crown of his head, he was supported in the water in such a way that his body and extremities could move freely while his nose and mouth were protected above the water level; (2) he was submerged in a prone

From the Normal Child Development Study of the Department of Pediatrics, Columbia University, and the Babies Hospital.

position without any support whatsoever; and (3) he was submerged without support in a supine position. The movements in each position were observed and described especially with respect to their organization, rhythmicity, and perseveration.

The movements of the infant only a few weeks old are striking when he is placed in water in a prone position. The baby usually remains in the prone position. Definite rhythmical associated flexor-extensor movements in upper and lower extremities together with a lateral flexion of the trunk corresponding to the flexor phase of the lower extremity are usually manifested. These movements are ordinarily sufficiently forceful to propel the baby a short distance through the water. The character of the movements is essentially the same whether the baby is supported under the chin or submerged in a prone position. Definite organization and rhythmicity of movements are, however, more pronounced when the infant is submerged. While similar to the reflex crawling and stepping movements which involve frictional hindrance, these swimming movements of the newborn infant are distinctly more synchronous and rhythmical. Even when the same infant is suspended in a prone position in air, and there is no friction with a hard underlying surface, his movements are not so rhythmical or organized as they are in water. Another outstanding feature of the infant's behavior during the newborn phase is breath control. Apparently a reflex inhibits his breathing while he is submerged, since he does not cough or show disturbances common among the older babies after they have been submerged. In fact, there seems to be a summation effect of the two reflex mechanisms since the neuromuscular activity is better integrated when respiration is inhibited, as indicated in the submerged situation. For the simple reason that the young baby remains in a prone position and engages in these rhythmical movements with sufficient force to propel his body forward through the water the term "reflex swimming movements" seems suitable to indicate this period. These rhythmical movements of the human infant are quite similar to those of other young quadrupeds in water.*

After the baby is 4 months of age or older, the rhythmicity and pattern of the early behavior become disorganized. Often the babies are quite inactive when supported under the chin, and when submerged prone they usually rotate into a dorsal position, and the movements of the extremities are of the struggling order. They clutch at the experi-

*For comparison we have studied the swimming behavior of the following mammals: (1) pouch young opossum ranging in length from 10 to 165 millimeters; (2) newborn rat, (3) kitten, (4) rabbit, (5) guinea pig, (6) *macacus rhesus* monkeys ages 5, 6, 15, and 340 days, and (7) one 2-month-old chimpanzee. All maintained the prone position and engaged in rhythmical movements of upper and lower extremities with the exception of the 2-month-old chimpanzee which was immobile and sank to the bottom, and the 15-day-old monkey, which maintained a vertical position in the water and whose movements were less organized and rhythmical than those of the younger monkeys. These observations suggest that the primitive reflex was beginning to disintegrate in this monkey by the time he was 2 weeks old. Observations should be made on a newborn chimpanzee before inference can be drawn as to the developmental status represented by the animal observed. This occasion is taken to express gratitude to Dr. Margaret A. Kennard for the privilege of photographing the primate behavior.

menter's hand, try to wipe the water from the face, or they may sink deeper into the water without marked manifestations of motor activity. Both the struggling activity and the comparative inertia are, for the sake of convenience, classed as representing the disorganized phase of development in this type of behavior. This phase, i.e., the struggling type of movement and the tendency to rotate from a prone to a dorsal position, continues as the most characteristic mode of behavior until about the time the baby is capable of independent erect locomotion. It was apparent during this phase that the baby had more noticeable difficulty with respiration, or controlling respiration, when he was submerged. Often the ingestion of fluid was considerable, and the infant would cough or otherwise show respiratory disturbance when he was taken out of the water.

Toward the beginning of the second year the child again shows a tendency to remain in the prone position, to engage in flexor-extensor movements of the extremities, especially the lower extremities, and to propel his body through the water. The quality of these movements is distinctly different from the rhythmical movements of the newborn; they are more deliberate and apparently of voluntary order. The child is not merely fighting; he is making purposeful movements, fairly well organized, but less automatic than the reflex movements, in order to gain the edge of the pool. At no time did any baby show himself capable of raising his head above the water level for the purpose of breathing.

In the dorsal position, with few exceptions, the disorganized or struggling movements were characteristic throughout the age range, and so the movements made when the child is submerged in the supine position do not show outstanding developmental changes. Although the baby engages in struggling movements, he does not rotate from a supine to a prone position. This observation on movements of the baby in a dorsal position probably explains why Watson found only "uncoordinated slashing of the hands and feet" in the aquatic behavior of the newborn.

The characteristic pattern of the newborn swimming movements is illustrated in the line drawings of Fig. 1 *A*. These drawings were obtained by tracing sequential projections of moving picture film in order to illustrate synergic movements. Fig. 1 *B* shows similar tracings representing the disorganized phase of the behavior pattern. It will be noticed in these drawings that the baby tends to rotate into a dorsal position and that there is no definite consistency or pattern in the consecutive movements. Fig. 1 *C* illustrates the deliberate movements of the ambulatory child. The impression gained from our observations of the children around this age is that without sustained swimming experience these movements subsequently become disorganized and the older child must learn to maintain the prone position for swimming. Sometimes these children, after making a few strokes in the prone position, would tend to assume a vertical position. Most children of 5 or 6 years whom

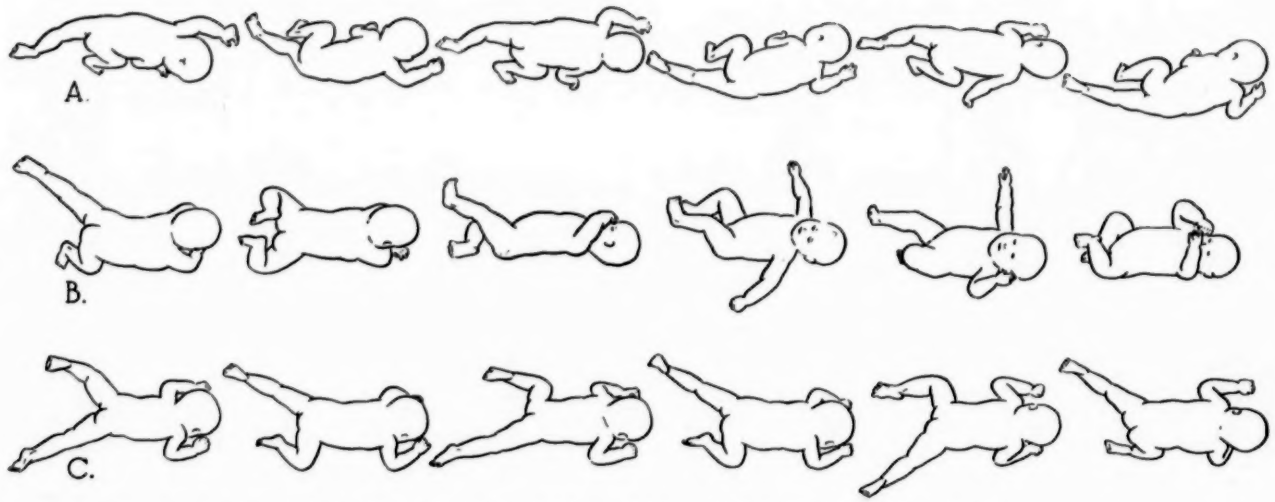


Fig. 1.—Line drawings representing three phases in the development of aquatic behavior of the human infant.
A. Reflex swimming movements.
C. Voluntary or deliberate movements.
B. Disorganized behavior.
These drawings were obtained by tracing successive frames of 16 mm. movie film illustrating the quality of consecutive movements made at different chronological or developmental stages.

the writer has had occasion to observe when they were learning to swim have shown a tendency to maintain an upright rather than a prone position in the water. This vertical position is probably an adaptive response for the purpose of getting the head above the water level. Apparently the ability to maintain the prone position in water is a definite phase in the achievement of swimming, and it is a characteristic, together with the quality of limb movements, which critically differentiates developmental phases in the growing infant.

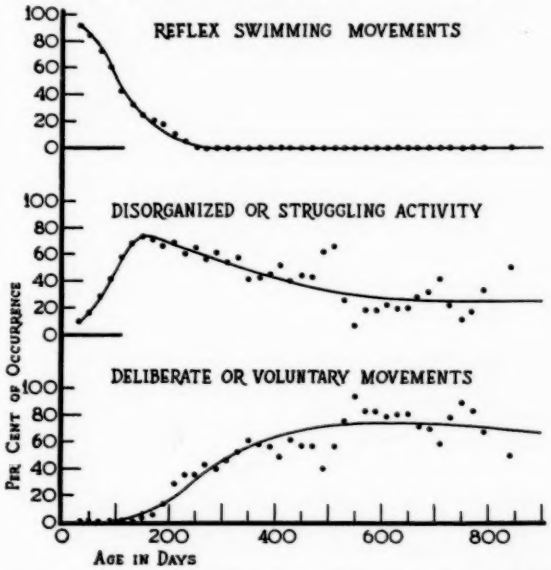


Fig. 2.—The incidence of three phases in the aquatic behavior of infants.

In order to show the general trend of development in aquatic behavior, the data on these 42 infants were tabulated on a plus-minus basis in chronological periods of 20 days. The results are indicated in the three curves (Fig. 2), showing (a) the decline of the reflex phase, (b) the period when disorganized behavior is most prominent, and (c) finally the period when the more deliberate movements are manifested. Since these curves represent group data, the phases are not so well differentiated as is the case when successive examinations of individual children are similarly analyzed. The scatter is the resultant of the fact that individual children vary considerably as to the inception and decline of different phases in the development of any activity. However, despite the scatter the decline of the reflex phase in this activity corresponds closely to the declining period of other atavistic reflexes, such as the Moro reflex, suspension grasp, crawling and stepping movements in the young infant.

INTERPRETATION

This study covers an analysis of the neuromuscular movements of infants when submerged in water. The manifestation in the newborn infant of a rhythmical, coordinated, reflex movement simulating the aquatic movements of other newborn mammals suggests functional evidence of the phylogenesis of man. The maturation of the central nervous system is reflected in the sequential changes of aquatic behavior as well as in other types of neuromuscular activity common to the human infant. It is interesting that developmental changes in swimming behavior correspond in chronological order to the major phases of other behavior patterns which also appear to be of phylogenetic origin.

REFERENCES

1. Watson, John: Psychology from the Standpoint of the Behaviorist, Philadelphia, 1919, J. B. Lippincott Company, p. 243.
2. McGraw, Myrtle B.: Growth, A Study of Johnny and Jimmy, New York, 1935, D. Appleton-Century Company, pp. 122-136.

STUDIES ON THE MENINGOCOCCUS AND MENINGOCOCCUS INFECTION

NELLES SILVERTHORNE, M.B., J. G. FITZGERALD, M.D., F.R.C.P.(C.), AND DONALD T. FRASER, M.B.

WITH THE TECHNICAL ASSISTANCE OF COLIN CAMERON
TORONTO, ONTARIO

INTRODUCTION

THERE is now an abundance of data on the various aspects of meningococcus infection in the epidemic form in adults. It is not the purpose of this communication to review in detail the literature on this subject. Certain researches, however, are of fundamental importance. The demonstration of the efficacy of antimeningococcic serum in reducing the mortality of meningitis was shown by Flexner.[1] Excellent monographs on many phases of meningococcus infection have been published by Netter and Debré,[2] Gordon,[3] Fildes and Baker,[4] Dopter,[12] and Murray.[13] During the years of the Great War other important contributions were made by FitzGerald,[5] Eastwood,[6] Griffith,[7] Scott,[8] Ponder,[9] Tulloch,[10] and Glover.[11] In the postwar period additional contributions have been published. Blackfan[14] reviewed the treatment of meningococcus meningitis. Studies on the types of meningococci isolated in the United States have been published by Branham and coworkers.[17] Outbreaks and epidemics have been reported and publications on serum therapy have appeared in recent years by Neal, Jackson, and Appelbaum,[15] Norton and Gordon,[16] Banks,[18] Walker,[19] Shaw and Thelander[20] (in children), Cantacuzène,[21] Tillett and Brown,[22] and Nicolau and others.[23] Observations of a similar nature during nonepidemic periods, however, are few (Cameron,[24] Dudley and Brennan,[25] and Rake[29]). The following communication is a report of clinical, epidemiologic, and bacteriologic observations made on cases of sporadic meningococcal meningitis occurring in children in and about Toronto from October, 1931, until May, 1938.

CLINICAL DATA

During the seven years under review 51 cases of meningitis were studied. From each of the patients *Neisseria meningitidis* was isolated from the spinal fluid, and the clinical picture left no doubt of the diagnosis. The patients varied in age from 22 days to 15 years. Postmortem examinations were made in 12 of the 21 fatal cases. In three instances there was basilar meningitis with definite evidence of meningococcal septicemia; that is to say, there was a hemorrhagic rash and

From the Connaught Laboratories, University of Toronto, the wards and laboratories of the Hospital for Sick Children, Toronto, and the Department of Paediatrics, University of Toronto.

petechiae in various organs. Four of the fatal cases of the acute type showed ventricular enlargement with hydrocephalus. In the remaining five cases, there was a more chronic type of basilar meningitis with hydrocephalus.

Clinical Course.—The patients were arbitrarily placed in one of three categories. *Fulminating cases* comprised those in which death occurred in 24 to 48 hours. *Acute cases* were the usual type seen in children during nonepidemic periods with a history of an acute onset and a duration of three to seven days. *Chronic basilar cases* were characterized by a history of one to three weeks' duration, definite opisthotonos, and signs of basilar involvement (Table I).

Complications.—The frequency and the type of complications are shown in Table II. It will be noted that the commonest was hydrocephalus, which occurred in 9 patients. This condition developed during the final stages of the disease; that is to say, after the acute symptoms had been present from six days to three weeks. All of these were patients under 7 years of age, and all died.

Treatment.—All cases were treated with polyvalent antimeningococcal serum which was usually administered by the continuous intravenous method[26] in doses of 20 c.c. to 150 c.c. during the first twenty-four to forty-eight hours after admission. In addition, daily intrathecal injections of serum totalling from 70 c.c. to 460 c.c. were given. The serum was supplied by the Connaught Laboratories and was not concentrated.

Mortality.—The gross mortality of the group was 42 per cent (see Table I). The mortality appears to depend to a great extent on the clinical type of the disease: in all those classified as "fulminating" and

TABLE I

MENINGOCOCCIC MENINGITIS

CLINICAL DATA

TYPES	NUMBER	RECOVERED	DIED	MORTALITY
Fulminating	6	0	6	100%
Acute	40	30	10	25%
Chronic basilar	5	0	5	100%
Total	51	30	21	42%

TABLE II

COMPLICATIONS

COMPLICATIONS	ACUTE PHASE		CONVALESCENCE		FINAL STAGES	
	NO.	NO. DIED	NO.	NO. DIED	NO.	NO. DIED
Hydrocephalus (9)	0	0	0	0	9	9
Strabismus (4)	4	0	0	0	0	0
Bronchopneumonia (4)	0	0	4	0	0	0
Iridochoroiditis (3)	3	0	0	0	0	0
Otitis media (2)	2	0	0	0	0	0
Pupillary paralysis (2)	0	0	2	0	0	0
Staphylococcic infections (3)	0	0	3	3	0	0
Cerebral thrombosis (1)	0	0	0	0	1	1

"chronic basilar" death resulted, whereas in a relatively high proportion of those cases classified as "acute" recovery occurred. Of the 10 fatal cases of the acute type 3 deaths were due to staphylococcal septicemia, staphylococcal meningitis, and staphylococcal brain abscess, respectively. If these 3 be deducted, the mortality in the "acute" group is reduced from 25 to 14 per cent.

BACTERIOLOGIC EXAMINATION

1. *Cerebrospinal Fluid.*—Cultures were obtained by planting the centrifugalized deposit from 5 to 10 c.c. of fluid directly into 1 per cent dextrose beef infusion broth and on to blood agar. The microorganisms were obtained from each of the cases under review, and no case has been included on clinical grounds alone. Identification of the microorganisms isolated was made by microscopic, cultural, and agglutination tests.

2. *Blood Culture.*—Ten cubic centimeters of blood obtained from the external jugular or median basilic vein were planted directly into 50 c.c. of 1 per cent dextrose broth, incubated overnight, examined microscopically, and subcultured on 10 per cent sheep's blood beef infusion agar. The original blood cultures were examined after 24 hours' incubation and re-examined at 48 hours and 72 hours. They were not incubated longer because experience had shown that this was valueless. In only 8 instances out of 28 in which blood cultures were made was *N. meningitidis* obtained. This is probably due to the fact that admissions to hospital were after the primary bacteriemic stage of the disease. In this connection it is noteworthy that the 8 positive results were obtained in patients who had presented symptoms for two or three days.

3. *Nasopharyngeal Cultures.*—West tube swabs were taken of the nasopharynx and the material was plated immediately on 10 per cent sheep's blood agar plates. The plates were incubated aerobically overnight; suspicious colonies were selected, examined microscopically, and subcultured on 10 per cent sheep's blood agar slopes. *N. meningitidis* was identified by microscopic, culture, and agglutination reactions.

TABLE III

SOURCE OF MENINGOCOCCI ISOLATED FROM PATIENTS

SOURCE	NUMBER	POSITIVE	NEGATIVE
Cerebrospinal fluid	51	51	0
Blood	28	8	20
Nasopharynx	24	24	0
Blood smears purpuric lesions	7	6	1

4. *Purpuric Spots.*—The lesions were punctured with a piece of sterile, broken, pointed glass after thorough cleansing of the skin. *N. meningitidis* was identified on a basis of morphology in the smears. No attempts were made to cultivate the organisms. Positive results were

obtained in 6 of the 7 examinations made (Fig. 1). A similar finding of the organisms in the purpuric spots has been recorded by McLean and Caffey.[27]

EPIDEMIOLOGIC DATA

Two series of investigations were carried out:—

(1) *Investigations on the Family From Which the Case Was Derived.*—The homes of 42 of the 51 patients were visited within a few days of the admission of the child to hospital. The environmental conditions were studied, and the clinical history of the contacts was obtained, and a bacteriologic examination of the nasopharyngeal cultures of the entire family was made.

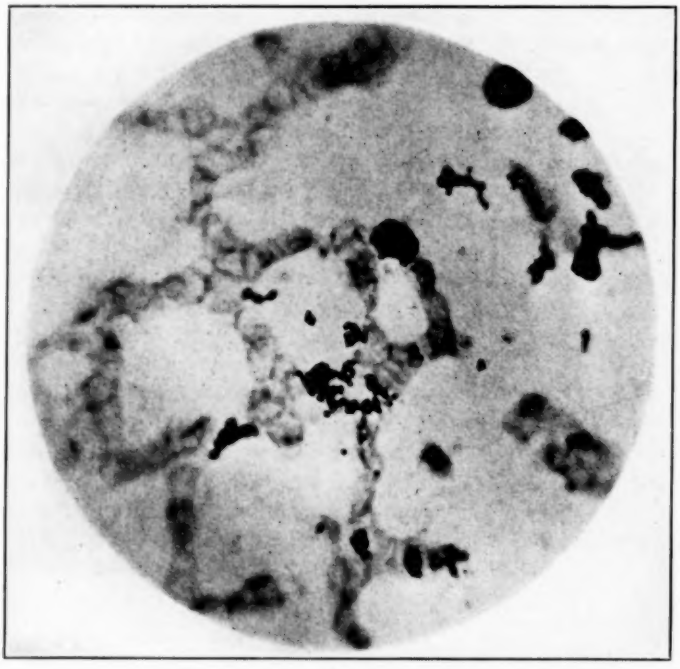


Fig. 1.—Organisms from purpuric spots.

Environment: The findings of the survey are given in Table IV. It is noteworthy that no less than 90 per cent of the patients came from homes which were poverty-stricken, in the worst residential quarters of the city. Overcrowding was the rule rather than the exception. The family in most instances was living in one or two rooms.

Race: There was no predominant racial incidence.

Season: The disease occurred mainly in the autumn, winter, and spring months of the year.

Previous Illness in the Family: No correlation was obtained between the occurrence of a case of meningitis and previous contact with meningitis by other members of the family. The incidence of upper respiratory tract infection was particularly studied. Twelve of the 42 "patient-contact" groups revealed a history of such infections. These infections were for the most part stated to be "colds" or "influenza."

Bacteriologic Examination of Contact Carriers: Nasopharyngeal cultures were taken of the contacts with West tube swabs, and the material was planted immediately on 10 per cent sheep's blood agar plates.

TABLE IV

EPIDEMIOLOGIC DATA

Number of families visited	42
Environmental conditions	
Overcrowding	37
Filth	19
Poor ventilation	18
Possible etiological factors	
Number with history of upper respiratory infection	12
Number of families with history of previous contact with a case of meningitis	3

TABLE V

EPIDEMIOLOGIC DATA:

BACTERIOLOGIC EXAMINATION OF CONTACTS

Total number of persons examined	327
Total number of positive cultures of the meningococcus	102
Percentage positive cultures	31
Number of families studied	42
Number of cases from these families	42
Number of families in which one or both parents were carriers	33
Number of families in which other members were carriers	3

The plates were subsequently spread at the laboratory and incubated aerobically overnight; suspicious colonies were picked, examined microscopically, and subcultured on 10 per cent sheep's blood agar slopes. *N. meningitidis* was identified by morphologic and cultural characteristics and agglutination tests. Table V summarizes the bacteriologic examination of these contacts. Thirty-one per cent of contacts were carriers of the meningococcus, and in 33 families of the 42 examined one or both parents were found to be carriers.

2. *Investigation on a Group of Healthy Adults Living in Toronto.*—Bacteriologic Examination: During four and one-half years of the seven-year study, nasopharyngeal cultures were examined monthly from a group of healthy adults who were not known to have been in contact with cases of meningitis. Similar bacteriologic technique was used as in the case of contact carriers. Table VII summarizes the findings. It will be observed that of the 2,378 swabs taken, 20 per cent were

positive for the meningococcus. The total number of individuals examined in the period of study was 70, and 32 of these individuals, or 45 per cent, were positive at one time or another. It may be noted, however, that the 20 per cent positive culture rate in the noncontact carrier group is only slightly lower than the 31 per cent found in the contact carriers examined.

TABLE VI

EPIDEMIOLOGIC DATA:

BACTERIOLOGIC ANALYSIS OF CASE AND CARRIER STRAINS

Number of families completely studied	33
Number of families in which case and carrier strains were identical	21
Number of families in which case and carrier strains were not identical	12

TABLE VII

EPIDEMIOLOGIC DATA:

BACTERIOLOGICAL EXAMINATION OF NORMAL INDIVIDUALS (NONCONTACTS)

Period of study	4½ years
Total number of swabs taken	2378
Total number of positive cultures obtained	499
Total number of individuals swabbed in 4½ years	70
Average number of individuals swabbed monthly	50
Percentage positive cultures	20

In this group of healthy adults it was found that certain individuals were persistent carriers over a matter of months and years, others carried the meningococcus intermittently, while others were transient carriers as noted before.[28] In 1936 Rake[29] found that a carrier might cease to harbor the meningococcus after an upper respiratory infection. We have also observed that the development of nasopharyngitis in a persistent carrier would often be followed by the disappearance of the carrier state; on the other hand, it was found that the onset of an upper respiratory infection in some individuals initiated the carrier state.

INVESTIGATION OF THE STRAINS ISOLATED

Strains of meningococci, 20 from cerebrospinal fluid, 17 from the nasopharynx of these cases, 1 from a case of meningitis with Type I meningococcus in the nasopharynx, 19 from the nasopharynx of contact carriers, and 22 from the nasopharynx of noncontact carriers, preserved, as soon after isolation as possible, in dried state in hard glass ampoules sealed under vacuum, were examined for virulence and type.

Determination of type was carried out by two methods. (a) A method described by Rake[30] was used as follows:

> All agglutinations have been carried out in water baths regulated to the required temperature. For antigen a standard suspension has been adopted consisting of a suspension of meningococci of a sufficient density to give a reading of 4 cm. when tested with a Gates turbidometer and corresponding to about 2,000,000,000 organisms per cubic centimeter.

Three-tenths cubic centimeter of this suspension is added to an equal amount of the serum or serum dilution to be investigated, the two fluids are mixed, and the rack of tubes is placed in the appropriate water bath for the required length of time. When a temperature of 37° C. is used, the tubes are removed after 2 hours and left in the icebox overnight, when a final reading is taken. The reading of the results must be largely a personal matter. In order to compensate for this, readings have been made by the same person throughout. A control tube with saline and suspension in equal parts is always inserted to detect salt sensitivity. When agglutinations are done at 56° C. for 24 hours or longer, a second control tube of normal serum diluted $\frac{1}{20}$ is added, but this has been found unnecessary at the lower temperature.

(b) The other method was an agglutination test carried out as follows:

Heat-killed saline suspensions of meningococci containing approximately 2,000,000,000 organisms per cubic centimeter were used as antigens. One-half cubic centimeter amounts of the antigen were added to the same volume of serial dilutions of Type I and Type II sera which were previously absorbed by a sufficiently large absorbing dose of meningococci ($\frac{1}{4}$ to $\frac{1}{2}$ c.c. of packed cells) to remove all Type II agglutinins from Type I serum and vice versa. The suspensions of meningococci in the type sera were then incubated at 56° C. in a water bath overnight. Readings were made the next day.

For some years we were frequently unable to allocate strains of meningococci to definite types with sera prepared from antigens of the four accepted types. Only by indirect typing, namely by preparing a rabbit serum from the strain to be typed and using cultures of the four types of meningococci as suspensions in agglutination tests, were we able to demonstrate that most of the strains isolated, early in the course of these studies, were Type II. In recent years we have used the two methods referred to and have failed to type certain strains, although other strains have fallen into clearly defined serologic types (Table VIII).

TABLE VIII

TYPE AND VIRULENCE OF STRAINS OF MENINGOCOCCI

NO.	SOURCE	TYPES			VIRULENCE								
		I	II	CROSS AGGLUTINATION WITH I & II DOUBTFUL	10	10^{-1}	10^{-2}	10^{-3}	10^{-4}	10^{-5}	10^{-6}	10^{-7}	10^{-8}
20	C. S. F.*	1	12	7							4	6	9
18	N.P.† cases	2	11	5						1	3	4	9
19	N. P. Contact carriers	1	15	3	1					2	0	4	12
22	N.P. Noncontact carriers	0	12	10	12	3					2	3	2
	Total	4	50	25	13	3				3	9	17	32

*C.S.F. = cerebrospinal fluid.
†N.P. = nasopharynx.

The two methods gave identical results in 36 per cent of the strains that were typed. In 28 per cent no agglutination occurred by the first method, but agglutination occurred with the second method. In 5 per cent of instances the type was obtained by the first method but not by the second. In no less than 31 per cent cross agglutination occurred to such an extent that we could not be certain of the type. The failure of the first method to type 28 per cent of strains is probably due to the fact that a low-titer serum was used. Most of the strains, 50 out of 79, were found to be Type II (Table VIII). Indeed, only four Type I strains have been isolated from the group studied; three of these were from meningitis patients and one from a carrier. Our results indicate that certain strains of meningococci are "narrow," and others are "broad" in respect of their agglutination in type sera. Branham[33] has demonstrated serologic diversity among strains of meningococci.

During the early years of our epidemiologic studies, typing of strains was carried out with unabsorbed four type sera. We were unable with this method to type the strains isolated. We were interested, however, in ascertaining whether contact-carrier strains were identical with case strains in our family groups. Strains from 33 family contact-carrier groups were studied in this way. The method used was the agglutinin absorption test as described by Butterfield and Neill[34] with the modification that a surplus of ¼ c.c. of packed cells was added to 2 c.c. of 1/50 dilution of each serum to ensure complete absorption of agglutinins. Table IX gives an example of strains which proved by test to be identical by agglutinin absorption.

TABLE IX

ANTIGEN	SERUM	DILUTION OF SERUM				
		1/100	1/200	1/400	1/800	SALINE CONTROL
A	+ A serum	4	4	4	3	0
A	+ A abs. A serum	0	0	0	0	
B	+ A abs. A serum	0	0	0	0	
B	+ A serum	4	4	4	3	0
B	+ B abs. A serum	0	0	0	0	
A	+ B abs. A serum	0	0	0	0	

It is quite obvious from this example that strains A and B are identical in respect of complete absorption of agglutinins from A serum. In two instances we resorted to reciprocal agglutinin absorptions and similar results were obtained. By this technique we were able to demonstrate that from 21 families we obtained carriers with strains identical with the case strain and in 12 families strains which were not identical with the case strains (Table VI). It is difficult to explain some of the discrepancies in the agglutinin absorption tests: in the twelve instances in which the strains were of the same serologic type but were not identical. Instances where the "parent strains"

were identical and other contact strains were not identical are also difficult to explain. If a large number of these contact-carrier strains had been "rough" variants and avirulent, the discrepancies might be accounted for (Wilson and Miles[37]). In only one instance was a strain "avirulent" and thus possibly a "rough" strain (Table VIII).

Determination of Virulence.—In examination of strains for virulence we have used the mouse-mucin test described by Rake.[31] The mice used in these experiments were obtained from one colony of Swiss white mice which gave uniform results. Each batch of mucin was tested for sterility before use and with a previously known virulent strain of the meningococcus and found in each instance to be satisfactory. From Table VIII it is seen that the vast majority (90 per cent) of strains obtained from the spinal fluid and the nasopharynx of these patients as well as from contact carriers possessed some degree of virulence. The virulence varied between 10^{-5} to 10^{-8} (10^{-8} contain approximately 20 meningococci). On the other hand, only seven of the 22 strains (32 per cent) recovered from noncontact carriers were found to be virulent in mice. The fact that the strains from noncontact carriers tend to be avirulent and those from contact carriers, virulent, is of considerable importance. In other words, 94 per cent of the case and contact-carrier strains are virulent as compared to 32 per cent in the noncontact-carrier group. In view of this, the rate of 31 per cent positive cultures in 327 contact carriers swabbed assumes greater significance than 20 per cent positive cultures in 2,378 swabs taken from the noncontact-carrier group. It is difficult to explain the finding that most strains in the contact-carrier group are virulent when many of them fail to show that they are identical in the absorption test.

In this connection reference may be made to the work of others in the examination of strains of meningococci isolated from the nasopharynx of healthy adults. Cameron[24] demonstrated a noncontact-carrier rate of 13 per cent in a group of 29 adults examined. Dudley and Brennan[25] reported a carrier rate of 50 per cent, persisting for over a year, in the absence of cases of meningitis among the personnel of naval and military establishments. In view of the fact that we have demonstrated that only 32 per cent of the cultures (7 out of 22) examined were virulent in a group of normal adults, it is possible that the carrier rates reported by Cameron[24] and Dudley and Brennan[25] do not represent the true percentage of carriers harboring disease-producing strains. Rake[29] contributed additional information on this subject by demonstrating that strains of Type II meningococcus are "frequent in the throats of normal individuals" not in contact with cases "during endemic periods." These Type II strains, however, Rake points out, "can also act as a parasite and produce sporadic cases of the disease." He states, however, that by and large most of these noncontact strains

of Type II are avirulent. These results are in complete agreement with our observations, and such researches suggest the necessity of testing the virulence of strains from cases, contacts and noncontacts before a proper evaluation of the carrier rate of potentially pathogenic strains may be arrived at or too many claims made for different therapeutic procedures.

In view of the fact that determination of the virulence of meningococci is a highly artificial method, the ability of meningococci to resist the bactericidal power of human blood has been employed in the hope that it would provide additional information as to the potential pathogenicity of the organism for man.

It was shown[35] that a cerebrospinal fluid strain of the meningococcus from a patient with meningitis survived to the limiting dilution (10^{-6}) in samples of bloods (citrated) of 11 infants and 8 of 33 adults. On the other hand, avirulent strains do not survive in any sample of citrated human blood.[36] It is true, as we have shown,[36] that strains virulent for mice are able to survive in human blood. But recently strains have been encountered (particularly those frozen and dried for one to three years) which have retained their mouse virulence but have lost their ability to resist the bactericidal power of human blood. It is evident therefore that the correlation between the two methods of test need not necessarily always hold. And it may well be that the method of assay in blood is a more reliable method for the assessment of pathogenicity for man than is the mouse-mucin test. On the other hand, the fact that strains which once survived in human blood and after storage do not may be interpreted as an indication of degradation of such strains.

It is quite evident that sporadic meningitis as it occurs in childhood is due to Type II meningococcus in which respect it differs from the adult epidemic form which is usually due to Type I meningococcus. This statement may find support from investigations that have been carried out during the past year.[32] Recently a Type I strain of the meningococcus (No. 520 obtained from Dr. Rake) was found to survive to the limiting dilution (10^{-6}) when grown with samples of blood from 7 different adults. On the other hand, 5 of these bloods were markedly bactericidal to a recently isolated and equally virulent Type II strain. One could advance the hypothesis from the examination of these two strains that although they were equally virulent for mice, the Type I strain would most likely be more pathogenic for a greater number of humans than the Type II strain.*

*This same hypothesis has been suggested in connection with pneumococcal infections in man in a recent publication by Maclean, Rogers, and Fleming.[38] These authors found that the sensitivity of different pneumococci to the antibacterial power of normal human blood is extremely variable. They state that "it is likely that this variation is related to the pathogenicity of these cocci in man."

DISCUSSION

There is thus much evidence that the incidence of virulent strains is higher among contacts than among noncontacts, and it is probable that the infection is derived from the former. It is also noteworthy that the majority of close contacts (parents) of the patients harbor meningococci of the same type and virulence. It must, however, be borne in mind that the carriers may have been infected by the case in their midst. This hypothesis is most unlikely in view of the history of upper respiratory infection in some of the carriers previous to development of the disease in the patient.

SUMMARY AND CONCLUSIONS

1. Fifty-one cases of three clinical types of meningococcic meningitis are reported. The mortality was 42 per cent. In 40 cases of the acute type the mortality was 25 per cent, and, if the three deaths from complicating staphylococcal infections be deducted, the mortality was 14 per cent.

2. Gram-negative diplococci were found in blood smears of the purpuric lesions in 6 of the 7 patients examined.

3. Forty-two families were visited and environmental conditions investigated.

4. In these families 327 contacts were examined for the presence of the meningococcus in their nasopharynx and 102 persons (or 31 per cent) were found to be harboring meningococci. The majority of these strains tested (94 per cent) were virulent for mice.

5. In 33 of the 42 families, one or both parents were found to be harboring meningococci.

6. In a period of four and one-half years, 2,378 nasopharyngeal cultures were examined from an average of fifty individuals monthly. No less than 20 per cent of the cultures were positive.

7. The majority of strains isolated from cases, contact carriers and noncontact carriers are Type II.

8. It is suggested from results of our experiments that the bactericidal power of human blood against the meningococcus or the ability of strains to survive in human blood may be as important in assessing the potential pathogenicity of a strain of the meningococcus for man as is an artificial mouse virulence test.

REFERENCES

1. Flexner, Simon: J. Exper. Med. **9**: 105, 1907.
2. Netter, A., and Debré, R.: La méningite cérébro-spinale, Paris, 1911, Masson & Cie.
3. Gordon, M. H.: Medical Research Council Special Report Series, No. 3, 1917.
4. Fildes, P., and Baker, S. L.: Medical Research Council Special Report Series, No. 17, 1918.
5. FitzGerald, J. G.: Canad. M. A. J. **6**: 695, 1916.
6. Eastwood, A.: J. Hygiene **17**: 63, 1918.

7. Griffith, F.: J. Hygiene **17:** 124, 1918.
8. Scott, W. M.: J. Hygiene **17:** 191, 1918.
9. Ponder, C.: J. Hygiene **17:** 247, 1918.
10. Tulloch, W. J.: J. Hygiene **17:** 316, 1918.
11. Glover, J. A.: J. Hygiene **17:** 350, 367, 1918.
12. Dopter, C.: L'infection méningococcique, Paris, 1921, Baillière et Fils.
13. Murray, E. G. D.: Medical Research Council Special Report Series, No. 124, 1929.
14. Blackfan, Kenneth D.: Medicine **1:** 139, 1922.
15. Neal, Josephine B., Jackson, Henry W., and Appelbaum, Emanuel: J. A. M. A. **87:** 1992, 1926.
16. Norton, J. F., Gordon, J. E., and others: J. Exper. Med. Vols. 4 & 5, 1930 and 1931.
17. a. Branham, Sara E., Taft, Clara E., and Carlin, Sadie A.: United States Treasury Dept., Public Health Reports **46:** No. 16, 1931.
b. Branham, Sara E., and Carlin, Sadie A.: J. Bacteriol. **34:** No. 3, 1937.
18. Banks, H. Stanley: Lancet **1:** 747, 1931.
19. Walker, W.: J. Roy. Army Med. Corps, Dec., 1932, Jan. and Feb., 1933.
20. Shaw, E. B., and Thelander, H. E.: J. A. M. A. **101:** 746, 1933.
21. Cantacuzène, J.: Office international d'hygiène publique **25:** Part II, 1216, 1933.
22. Tillett, William S., and Brown, Thomas McPherson: Johns Hopkins Hosp. Bull. **57:** 297, 1935.
23. Nicolau, I., and others: Arch. roum. de pathol. expér. **9:** 365, 1936.
24. Cameron, D. W.: Trans. Roy. Soc. Canad. **25:** Section V, 97, 1931.
25. Dudley, S. F., and Brennan, J. R.: J. Hygiene **34:** 1935.
26. Silverthorne, N.: J. PEDIAT. **9:** 755, 1936.
27. McLean, S., and Caffey, J. P.: Am. J. Dis. Child. **35:** 357, 1928.
28. Silverthorne, N.: J. PEDIAT. **9:** 328, 1936.
29. Rake, G.: Canad. Pub. Health J. **27:** 105, 1936.
30. Rake, G.: J. Exper. Med. **57:** 561, 1933.
31. Rake, G.: J. Exper. Med. **61:** 545, 1935.
32. Silverthorne, N.: Studies on the Bactericidal Power of Human Blood (Unpublished).
33. Branham, Sara E.: J. Immunol. **23:** 49, 1932.
34. Butterfield, C. T., and Neill, M. H.: Treasury Dept., United States Public Health Service Hygienic Laboratory Bull. 124, 1920.
35. Silverthorne, N., and Fraser, D. T.: Brit. J. Exper. Pathol. **15:** 362, 1934.
36. Silverthorne, N., and Fraser, D. T.: J. Immunol. **31:** 43, 1936.
37. Wilson, G. S., and Miles, A. A.: Brit. J. Exper. Pathol. **13:** 1, 1932.
38. Maclean, Ian H., Rogers, Keith B., and Fleming, Alexander: Lancet, March 11, 1939.

THE DETERMINATION OF VITAMIN C IN CHILDREN BY INTRADERMAL INJECTION

HOWARD G. RAPAPORT, M.D., AND SIDNEY H. MILLER, M.D.
NEW YORK, N. Y.

ROTTER[1] first attempted to show that an intradermal skin test performed with 2:6 dichlorphenolindophenol may be employed as a method for the determination of vitamin C in the living organism. He studied the test on guinea pigs, in that he injected intradermally a small measured quantity of this dye substance and observed the length of time necessary for decolorization to take place. Rotter concluded from his experiments that the time for decolorization of the dye was an indication of the degree of saturation with vitamin C of the organism. He stated that if the test animal was saturated, the dye disappeared in less than five minutes; in normal cases from five to ten minutes elapsed. In deficient cases more than ten minutes were required for decolorization. Portnoy and Wilkinson[2] repeated Rotter's test on a series of 103 children and adults and were satisfied with the value of this test. The value of this test was first shown to be clinically questionable by Poncher and Stubenrauch.[3]

We began our experimental studies with animals. A 1/400 normal dye solution was injected by a 1.0 ml. tuberculin syringe into the skin of the shaven abdomens of healthy rabbits whose vitamin C contents were normal. Wheals approximately 2 mm. in diameter were produced. As a control, we injected a similar amount of methylene blue dye solution. The 2:6 dichlorphenolindophenol dye solution disappeared within five minutes whereas the methylene blue dye solution remained unchanged for at least twenty-four hours, showing that the dye was not absorbed but disappeared, probably by reduction in the tissue. This same dye in vitro is reduced by cevitamic acid, whereas methylene blue remains unchanged when titrated with cevitamic acid.

METHOD OF PREPARATION OF THE DYE SOLUTION AND TECHNIQUE OF THE TEST

The method used for making the dye was described by Rotter. A sterile solution containing 2 mg. of the powdered dye 2:6 dichlorphenolindophenol in 4.9 c.c. of distilled water was used for the intradermal test. To prepare the solution, the proportions used were 4 mg. of the dye dissolved into 4.9 c.c. of sterile distilled water. This solution was passed through a Seitz filter for sterilization. During the process of filtration 20 per cent of the dye was lost. To determine the reducing value of the dye filtrate, a small portion of this sterile dye is retained and titrated against a standardized cevitamic acid solution. Another solution of 2 mg. of the

From the Pediatric Department, Mount Sinai Hospital, Dr. Bela Schick, Director.

2:6 dichlorphenolindophenol dye in 4.9 c.c. of water is also titrated against this standard cevitamic acid. The sterile filtrate of dye solution is then diluted with sterile water to correct its strength to the proportion of 2 mg. of dye to 4.9 c.c. of distilled water. Every seven days, the dye solution is freshly prepared because after this time the dye begins to deteriorate. The injections are made intradermally on the extensor surface of the thigh about six inches above the knee. This area was chosen because, in case the dye solution should for some reason fail to be reduced, it would leave a blemish in an inconspicuous site. The area was cleansed with alcohol, allowed to dry, and then a small wheal 1 mm. in diameter was made with the dye solution. Immediately preceding the intradermal injection, 2 c.c. of blood was taken from the vein and the cevitamic acid of this was determined at once by the Farmer and Abt[4] method. Portnoy and Wilkinson raised four small wheals and took the average time of disappearance for their timing. We did this with our rabbits and found the time variation to be very slight whether one or four wheals were made. We decided therefore to use only one wheal. This procedure decreases the trauma and pain to the patient. The intradermal injections were always done by the same person thereby eliminating the differences in measurement due to different observers.

RESULTS

We have tested 100 children, febrile and afebrile, picked more or less at random from the wards and out-patient department of Mount Sinai Hospital. In this series, some of the children have been retested after large amounts of cevitamic acid had been given by mouth to them over a period of two weeks. We divided our results into three groups.

Group 1. Those with low blood vitamin C content, or the scorbutic group.

Group 2. Those with a subnormal blood vitamin C content, or suboptimal.

Group 3. Those with a normal or high blood vitamin C content or saturated group.

Group 1 comprised 26 per cent of our cases. The blood vitamin C content of this group ranged from 0.19 mg. per cent to 0.5 mg. per cent, and the decolorization time of the dye injected intradermally ranged from 2.5 to 30 minutes with only three of these over ten minutes or below.

Group 2, or the suboptimal group, comprised 21 per cent of our cases. Blood vitamin C contents in this group fell between 0.5 mg. per cent and 0.7 mg. per cent. The decolorization time of the dye in this group varied from three minutes to twenty minutes, with two being above ten minutes, five being between five and ten minutes, and fourteen being at five minutes or less.

In Group 3, or the saturated group, we find the majority of our cases, 53 per cent in all. The time varied from two to twenty minutes. Only one of these children had a decolorization time of over ten minutes, 19 between five and ten minutes, and 33 five minutes or less.

A total of 6 per cent of the children had decolorization times over ten minutes, and only half of these were in the scorbutic group. Thirty

TABLE I

DECOLORIZATION TIMES IN CONTRAST TO BLOOD PLASMA CEVITAMIC ACID LEVEL IN EACH CASE

PATIENT	CEVITAMIC ACID LEVEL IN BLOOD PLASMA MG. PER 100 C.C.	DECOLORIZATION TIME IN MINUTES
Group 1	*Low Blood Vitamin C Level*	*Range Below 0.5 mg. %*
H. V.	0.19	3
R. D.	0.28	8
A. K.	0.28	5
A. C.	0.40	5
G. W.	0.35	5
S. B.	0.29	30
S. B.	0.39	15
N. L.	0.42	8
C. F.	0.24	5
S. B.	0.35	5
A. N.	0.34	2.5
M. M.	0.36	5
C. B.	0.36	5
S. J.	0.32	7
S. C.	0.19	7
E. C.	0.30	6
H. S.	0.24	9
F. A.	0.48	5
Y. K.	0.48	3
C. S.	0.32	4
D. M.	0.24	5
M. G.	0.24	15
M. K.	0.31	5
J. R.	0.41	4.5
V. Z.	0.50	2.5
H. V.	0.40	4.5
Group 2	*Range 0.5-0.7 mg. %*	
D. S.	0.59	4
E. C.	0.70	7
A. B.	0.65	3
C. B.	0.68	2
S. B.	0.60	20
S. B.	0.56	11
S. B.	0.56	4
C. F.	0.56	3
C. F.	0.68	3
S. B.	0.69	8
J. R.	0.64	6
W. B.	0.64	5
M. S.	0.58	4
C. M.	0.56	6
M. G.	0.64	8
R. M.	0.64	3
C. S.	0.53	3
E. L.	0.61	4
H. L.	0.61	4
S. F.	0.51	3
A. S.	0.68	5

TABLE I—CONT'D

PATIENT	CEVITAMIC ACID LEVEL IN BLOOD PLASMA MG. PER 100 C.C.	DECOLORIZATION TIME IN MINUTES
Group 3	*Low Blood Vitamin C Level*	*Above 0.7 mg. %*
I. L.	0.88	5
V. Z.	0.88	3
A. N.	0.98	7
A. N.	1.12	4
H. K.	0.84	5
J. S.	1.80	5
E. R.	0.80	8
A. N.	0.80	6
T. P.	0.80	7
C. S.	0.80	5
A. A.	1.00	5
Y. S.	1.60	6
D. K.	1.00	4
H. S.	1.00	4.5
N. S.	3.50	5
A. T.	0.98	8
S. B.	0.84	5
S. B.	1.96	6
N. L.	1.20	7
C. F.	0.84	4.5
N. L.	0.84	5
C. F.	0.84	5
A. N.	1.12	4
N. L.	0.84	7
C. F.	1.68	6
C. B.	0.88	7
N. L.	0.78	7
N. L.	1.21	7.5
C. F.	0.86	3.5
A. N.	0.78	4.5
J. C.	1.33	3
W. K.	1.07	4
P. S.	0.71	4
P. F.	0.89	4
M. O.	0.81	8.5
S. C.	0.81	4.5
M. G.	0.71	4
P. G.	0.81	5
A. P.	1.02	6
F. H.	0.80	6
S. K.	0.80	6
H. L.	1.50	3
I. L.	1.30	4
H. E.	1.00	4
D. S.	1.80	5
M. S.	1.03	2
S. V.	1.00	4
T. F.	1.80	4
S. R.	1.80	5
D. D.	0.80	20
F. G.	0.88	4
M. M.	0.88	4
E. J.	0.93	8

per cent required five to ten minutes, and only one-sixth of these were in the scorbutic group. Sixty-four per cent of the children had decolorization times of five minutes or less; more than one-fourth of these were in the scorbutic group.

CONCLUSION

We feel that this intradermal test for the determination of the amount of vitamin C in the body is not of significant value.

It was in the saturated group that we found that the test gave us a fair indication of the state of saturation. However, the test, in order to be of value must be applied generally and must include both vitamin C saturated and unsaturated children. It has failed in the unsaturated group to give us accurate information concerning the degree of vitamin C deficiency.

SUMMARY

A series of 100 children were injected intradermally with a dichlorphenolindophenol solution, and a bluish wheal was produced. The length of time for the blue color to disappear was noted. The cevitamic acid of the blood plasma was determined by the Farmer and Abt method, and we attempted to correlate the time taken for the dye substance to decolorize with the amount of vitamin C in the blood plasma. There is no satisfactory correlation which can be used for clinical purposes.

REFERENCES

1. Rotter, H.: Nature, London **139**: 717, 1937.
2. Portnoy, B., and Wilkinson, J. F.: Brit. M. J. **1**: 328, 1938.
3. Poncher, H. G., and Stubenrauch, C. H., Jr.: J. A. M. A. **111**: 302, 1938.
4. Farmer, C. J., and Abt, A. F.: Proc. Soc. Exper. Biol. & Med. **34**: 146, 1936.

ALLERGOMETRIC TUBERCULIN STUDY

HERMANN VOLLMER, M.D., CARL ZELSON, M.D., AND HAROLD RUBIN, M.D.
NEW YORK, N. Y.

IN 1934 von Groer[1, 2] described a new method of prognosticating the course of tuberculosis in childhood. In testing children allergic to tuberculin with several intracutaneous tests of varying tuberculin concentrations, he found that the degree to which the concentration of tuberculin affects the strength of the reaction varies greatly with the individual. He differentiated the following types of relationships between the degree of reaction and the concentration of the tuberculin: (1) In some children the strength of the reaction diminished as the concentration of the tuberculin was decreased, so that on the basis of the clinical appearance of the reaction, a proportional relationship between the extent of the reaction and the tuberculin concentration could be assumed; (2) in other children he found that repetition of the same experiment yielded results which indicated that there was no such simple proportional relationship. He found that the reactions were either relatively too great or relatively too small. On the basis of his results, he feels that there is a quantitative relationship between the size of the reaction and the tuberculin concentration used. He also believed that the tuberculin reaction indicates the relationship between reactivity and sensitivity to the injected tuberculin, and thus the state of allergy present. This in turn indicates, in von Groer's opinion, the degree of tuberculosis and its activity.

One of us (Zelson[3]) has repeated this work in a series of about three hundred children over a period of four years; his results, however, have not yet been published.

In attempting to produce a simple allergometric procedure, Vollmer introduced the allergometric tuberculin patch test as described in a recent publication on tuberculin patch therapy by Vollmer and Goldberger.[4] This patch test was used for a rough determination of the individual tuberculin sensitivity before the tuberculin patch therapy was instituted. In our present study the patch test has been compared with von Groer's allergometric method only in a limited form. It could not be compared from the quantitative point of view, because the exact amount of tuberculin absorbed could not be determined. With reactions to patch application of tuberculin one cannot use the usual linear measurements, but must merely call the test either highly positive, positive, or negative. Since the patch test method is less cumber-

From the Pediatric Service of Sea View Hospital, Dr. Bela Schick, Director.

some and, in addition, less disagreeable and painful for the patient, it could replace the intracutaneous method if a fair conformity between the two could be established.

The allergometric patch test is prepared in the following manner:* Upon an adhesive strip are placed five small pieces of filter paper located about 1 cm. from each other. Each piece of filter paper is saturated with tuberculin of gradually decreasing concentrations of full strength, 1/2 strength, 1/4 strength, 1/20 strength, and 1/100 strength. The tuberculin is prepared on a synthetic medium.[6] This strip containing the five dried filter papers is applied to the skin for 48 hours; the reaction is read 48 hours later. It is not a quantitative test as mentioned before, since the amount of absorbed tuberculin cannot be judged and depends, to a degree, on the individual structure of the skin and on the amount of sensible and insensible perspiration. Nevertheless we feel that this is a very simple method which, as we shall show later, is sufficiently exact for estimating the approximate skin sensitivity to tuberculin.

PROCEDURE

In the present study we have compared the allergometric tuberculin patch test with the intradermal method of von Groer. The cases were selected from patients at the Sea View Hospital, New York, and consisted of a group of 106 children with active tuberculosis (Table I). At the same time, intradermal injections of 0.1 c.c. of a 1:10,000 dilution of tuberculin and a like amount of 1:1,000,000 dilution of tuberculin were made on the volar surface of the forearm. The weaker dilution was injected at an angle, below the stronger dilution. This was done to avoid the possibility of absorbed tuberculin draining upward via the lymphatics and increasing the reaction of the test above. New tuberculin syringes and new needles were used in doing all the tuberculin tests. Extreme care was taken to insure that the correct dosage be injected. Dilutions of the tuberculin were freshly prepared on the day of testing. The tuberculin used was that distributed by the New York City Department of Health. The patch test was removed 48 hours after application, and the result was read 48 hours after the removal of the patch. The intradermal tuberculin tests were read and measured at the end of 48 hours. Each intradermal tuberculin reaction was measured by taking the arithmetical mean of the two largest diameters as the size of the reaction. In order to have a definite edge of demarcation for the measurement of the size of the reaction, only the area of infiltration and redness was measured.

TABLE I

NO. OF CASES	REACTIONS TO THE MANTOUX TESTS		REACTIONS TO THE ALLERGOMETRIC PATCH TESTS				
	1:1,000,000	1:10,000	5+	4+	3+	2+	1+
73	More than 5 mm. in diameter	More than 5 mm. in diameter	21	35	13	2	2
33	Negative	More than 5 mm. in diameter	0	6	14	8	5
Total 106			21	41	27	10	7

*Available from Lederle Laboratory, New York, N. Y., for experimental purposes.

All the tests were interpreted and measured by each of the three men doing this work. Where there was any discrepancy, the results were rechecked and a definite conclusion arrived at by agreement of all three.

In Table I we have summarized the results of the tests in the entire group of the 106 children. We have used the terms one-plus to five-plus, but not with the usual interpretation. By one-plus is meant a positive reaction to only one of the squares on the patch test; two-plus means that the skin reacted to two of the squares on the patch test, etc. From Table I it is evident that:

1. There is 100 per cent qualitative conformity between both methods.

2. Cases with positive Mantoux reactions to the dilution 1:1,000,000 show, in the main, a reaction to four or all five of the allergometric patches.

3. Cases with negative 1:1,000,000 Mantoux reactions but with positive 1:10,000 Mantoux reactions show frequently only reactions to one, two, or three of the patches which contain the higher tuberculin concentrations. Only a few react to the fourth patch. The reaction to the fifth patch containing the weakest tuberculin concentration is always negative.

4. Reactors to four or all five patches are characterized by a very high tuberculin sensitivity corresponding approximately to a sensitivity to the 1:1,000,000 tuberculin dilution in the Mantoux test.

5. Reactors to only one, two, or three patches indicate a lesser tuberculin sensitivity.

In further analyzing our cases we divided the entire group into five subdivisions, on the basis of clinical and x-ray evidence of the tuberculosis present (Table II). The five groups were (1) primary complex; (2) primary infection with only tracheobronchial glands evident on x-ray; (3) tracheobronchial glands with an associated

TABLE II

GROUP	DIAGNOSIS	NO. OF CASES	REACTIONS TO THE MANTOUX TESTS		REACTIONS TO THE ALLERGOMETRIC PATCH TESTS				
			1:1,000,000	1:10,000	5+	4+	3+	2+	1+
1	Primary complex	20	17	20	6	9	3	1	1
2	Tracheobronchial glands	10	8	10	3	4	1	2	0
3	Tracheobronchial glands and pleural effusion	14	6	14	1	8	1	1	3
4	Bone, joint, and gland tuberculosis	19	18	19	8	5	5	1	0
5	Advanced progressive tuberculosis	43	24	43	3	15	17	5	3
	Total	106	73	106	21	41	27	10	7

pleural effusion; (4) bone, joint, and gland tuberculosis; and (5) far-advanced progressive tuberculosis. In the first group there were twenty patients, seventeen of whom reacted to the 1:1,000,000 dilution of tuberculin and fifteen who gave a four- or five-plus reaction to the patch test. In the second group there were ten patients, of whom eight reacted to the 1:1,000,000 dilution of tuberculin and seven gave a four- or five-plus reaction to the patch test. There were fourteen children in the third group; of these, six reacted to the 1:1,000,000 dilution, and nine gave a four- or five-plus patch test. There were nineteen cases in the fourth group; of these, eighteen reacted to the 1:1,000,000 dilution, and thirteen gave a four- or five-plus patch test. In the fifth group there were forty-three cases; twenty-four of these gave a positive test to the 1:1,000,000 dilution, eighteen gave a five- or four-plus patch test, and thirty-two of the children gave a three- or four-plus patch test.

From the above it is quite apparent that the children in whom there is evidence of a primary complex on x-ray, and those who present bone, joint, or gland tuberculosis are the most sensitive to tuberculin, both to the Mantoux test and to the patch test. The children with advanced progressive tuberculosis are obviously the least sensitive to tuberculin.

DISCUSSION

A negative tuberculin test in a tuberculous child may mean either a state of negative or positive anergy and thus mean an unfavorable as well as a favorable condition. Accordingly, all the intervening degrees of tuberculin sensitivity, from an extremely weak reaction to an extremely strong one, may have diverse meanings in each individual case. However, active cases present, in general, a higher tuberculin sensitivity than inactive cases; skin, bone, and gland tuberculosis, likewise, show relatively high tuberculin sensitivity. Therefore, a certain clinical value must be conceded to allergometry. The present degree of tuberculin sensitivity and its changes, in conjunction with other clinical signs and symptoms, will direct the physician to a more proper prognosis and therapeutic approach to the patient.

Because of our present findings and our past experience with tuberculous children, we feel that the tuberculin test should not be taken as the only guide to the activity of the tuberculosis present. The degree of tuberculin sensitivity may be of some significance when considered in association with the clinical and x-ray findings. We have come to the conclusion that the allergometric patch test, like the Mantoux test, can give adequate information of the state of tuberculin sensitivity in the individual child and that repeated patch tests will easily show the course of the tuberculin sensitivity.

SUMMARY

1. One hundred and six children with active tuberculosis have been tested, by varying dilutions of intracutaneous tuberculin and by an allergometric patch test administered simultaneously.

2. The allergometric tuberculin patch test is described, and its value in testing is discussed.

3. The allergometric patch test compares favorably with the intradermal tuberculin test in that the results tend to show that generally individuals who react to the weakest dilution of the tuberculin given intradermally also react to the weakest solution in the filter paper patches.

4. The severity of the tuberculin reaction does not indicate the severity of the tuberculous process in a group of children with active tuberculosis.

5. The allergometric patch test could replace the original patch test,[5] since it has the same qualitative value, and in addition, gives some quantitative information with regard to the individual sensitivity; if repeated at intervals, it will show the course of the tuberculin sensitivity.

REFERENCES

1. von Groer, F.: Wien. klin. Wchnschr. **47**: 1281, 1934.
2. von Groer, F.: J. PEDIAT. **6**: 297, 1935.
3. Zelson, Carl: To be published.
4. Vollmer, H., and Goldberger, E. W.: Bull. Sea View Hosp. **4**: 317, 1939.
5. Vollmer, H., and Goldberger, E. W.: Am. J. Dis. Child. **54**: 1019, 1937; **56**: 584, 1938; and **57**: 1272, 1939.
6. Siebert, F. B.: Am. Rev. Tuberc. **30**: 713, 1934.

25 CENTRAL PARK WEST
498 WEST END AVENUE
SEA VIEW HOSPITAL

SOME PROBLEMS OF DIPHTHERIA IMMUNIZATION

MAURICE M. HILLMAN, M.D., DR. P. H., AND JOSEPH I. LINDE, M.D.
NEW HAVEN, CONN.

MANY papers have been published and a considerable amount of statistical data has been accumulated to prove the value of toxoid as an immunizing agent against diphtheria since Ramon of the Pasteur Institute first introduced it in 1923, under the name of anatoxin. Therefore, it does not require further discussion.

Although there has been some claim that the Schick test is not entirely adequate as an exact measure of immunity to diphtheria, its practical value in the determination of susceptibility to the development of clinical diphtheria in most cases is established. Maloney and Fraser[1] sum up the situation by stating that negative reaction may be taken as presumptive evidence of immunity to diphtheria, but not as a guarantee of immunity. In this study we assume that toxoid is the most widely accepted agent in diphtheria immunization and that the Schick test is the only practical means by which we can determine whether an individual is immune as a result of injection of toxoid or has natural immunity.

Since the introduction of toxoid, however, problems have developed in connection with diphtheria immunization which are of practical interest both from the administrative point of view and from the point of view of the physician in private practice. Some of these factors to consider are as follows:

1. Age factor in relation to immunity.
2. Time relationship between immunization and the Schick test reaction.
3. Problem concerning the reversal from Schick-negative to a Schick-positive.
4. Effect of injection of two doses of toxoid in comparison with three.

The first problem which still remains to be solved, and regarding which there has been controversy, is the age factor in relation to immunity. There has been considerable discussion and disagreement as to which is the most favorable or desirable age at which immunization against diphtheria should be carried out. Disagreement also exists as to whether there is more lasting immunity when the child is immunized at 6 months or at 9 months of age. In private practice many pediatricians advise active immunization at 10 months of age. Public Health administrators on the other hand, advocate immunization at 6 to 9 months of age.

From the Department of Health, New Haven.

There are two factors which must always be considered when immunization at an early age is advocated: (1) the fact that young infants generally form antitoxin to a slight extent; and (2) the fact that a large percentage of infants still retain their passive immunity inherited from their mother. Greengard[2] has shown that very young infants form antibodies more slowly than older children. McKahnn and Kapnick in a recent article[3] state that the newborn infant is immune to many diseases by reason of passive transfer of antibodies from the mother. After the passive immunity is lost, the child becomes susceptible—more susceptible than the older child. This susceptibility appears to depend upon a deficiency in the ability to produce antibodies. The deficiency is associated with a similar low level of natural antibodies such as isoagglutinins and heterophile antibodies.

From this it appears that a reduced response to active immunization must be expected in infants and that a further diminution in response occurs if immunization is attempted before the natural immunity is lost. Thus toxoid administration against diphtheria will produce a larger percentage of immunizations if it is done after the passive immunity derived from the mother is gone and if it is done late in infancy, when immunizing power is riisng. The young child seems to respond even better than the infant, but undue delay must be weighed against the possible danger of exposure in the older patient. Thus immunization against diphtheria may be delayed until late in the first year of life without material increase in danger to the infant and with much greater immune response than would be obtained from earlier inoculation.

Park has shown that toxin-antitoxin injected before the sixth month and even later is inadvisable in the presence of passive immunity, and he ascribed the failure of the production of antitoxin in such individuals to over neutralization.[4]

Greengard[5] recently has shown that in a group of infants tested, 68 per cent of the babies will show a negative test at six months, while at from nine months to one year 70 per cent are positive. This is in agreement with the mass of statistical evidence that has been gathered. In a more recent study Greengard and Berstein[6] conclude that passive immunity in infants interferes with the development of antitoxin in response to vaccination with diphtheria toxoid and that immunization, therefore, should not be done in young age groups without preliminary Schick testing.

Benjamin and associates[7] recently made a study of Schick testing and concluded that there is nothing whatever in their data to suggest or to support the contention of Ramon and Debré that younger children are not as readily immunized as older children. The authors, however, admit that the number of children under 1 year of age was very small and hence, definite conclusions could not be drawn. Most of the children they tested were 1 year of age.

Blum in a recent study states that it is hazardous as a public health measure to inoculate children under 9 months of age, without preliminary Schick testing.[8] Benjamin and co-workers,[7] on the other hand, contend that it appears to be safe and economically sound in a public health program in a large city, to omit Schick testing for young children after, as well as before, active immunization to diphtheria by the administration of three doses of toxoid. So much, then, for the age factor in relation to immunity.

The second problem is that concerning the time relationship between immunization and the Schick test reaction. At present, it is the rule to make Schick tests six months after immunization. In reviewing the literature, one is struck with the paucity of material in regard to this question. It would be of interest to know what is the period of greatest titer after immunization: whether by doing the Schick test one year instead of six months after immunization, it would be possible to obtain a better gauge or a more complete picture as to the immunity conferred. Benjamin and his collaborators have shown that there is a decline in the ability to give a negative Schick reaction as the time interval between the last dose of toxoid and the Schick test is prolonged.

Another important and practical problem is that concerning the reversal from a Schick-negative to a Schick-positive. Here, too, very little work has been done in this respect.

The fourth problem relates to the question as to whether three doses are more effective than two doses of toxoid. The consensus of opinion at the present time seems to favor the three doses. Ramon and his co-workers[9] found that in general, better results were obtained when three injections were given. Their recommended dosage at present consists of three injections of 0.5, 1, and 1.5 c.c. of diphtheria toxoid, with an interval of three weeks between the second injection and two weeks between the second and third. Benjamin and his associates[7] found that three doses induced a higher degree of immunity, as gauged by the Schick test, than two doses of toxoid. The same investigators claim that the immunizing interval can be varied within fairly wide limits without interfering with the resulting immunity so far as the Schick test shows. The percentage of negatives, as the result of this type of immunization (3 dose), is 96 per cent. Fitzgerald and his associates[10] in a recent study have demonstrated that three doses of unmodified diphtheria toxoid induced a higher degree of antitoxin response than any of the procedures compared, namely, two doses of unmodified diphtheria toxoid, one dose of alum-precipitated toxoid and two doses of alum-precipitated toxoid. The doses were 0.5, 0.5 and 1 c.c. of diphtheria toxoid given at intervals of three weeks.

In view of these controversial questions, it was believed that if an analysis of the past experiences with the diphtheria toxoid immunization

in New Haven were to be undertaken, some of these problems might be solved. At the suggestion of one of us (J. I. L.) this study was made. The material consisted of three groups of children:

1. One group—987 children who had been immunized with two doses of toxoid, one month apart—ages ranging from six months to one year.

2. Second group—187 children who had been immunized with 1 c.c. of alum-precipitated toxoid (one dose)—ages ranging from six months to five years of age.

3. Third group—180 children who had been immunized with two doses of toxoid, one month apart—ages ranging from six months to five years of age. This group was Schick-tested again (Dr. Hillman) after having once been found negative.

The following are the results obtained:

Tables IA and IB show a group of children classified according to sex and age. These tables show further the age period at the time of immunization and the percentage of Schick-negatives obtained. According to these tables, it is evident that a definite relationship exists between sex

TABLE I

RESULTS OF 2 DOSE TOXOID IMMUNIZATION IN CHILDREN 1 YEAR OR UNDER

A. PERCENTAGE OF CHILDREN GIVING A NEGATIVE SCHICK TEST ACCORDING TO AGE, SEX, AND DOSE

AGE IN MONTHS AT TIME OF IMMUNIZATION	MALES			FEMALES			BOTH SEXES		
	NEG.	POS.	% NEG.	NEG.	POS.	% NEG.	NEG.	POS.	% NEG.
6	108-	10	91.5	91	20	82.0	199	30	86.9
7	92	15	86.0	71	12	85.5	163	27	85.8
8	71	12	85.5	60	14	81.1	131	26	83.4
9	55	7	88.7	35	18	66.0	90	25	78.3
10	20	11	64.5	44	8	84.6	64	19	77.1
11	30	8	78.9	24	13	63.9	54	21	72.0
12	40	13	75.5	41	14	74.5	81	27	75.0
Total	416	76	84.5	366	99	78.7	782	175	81.7

B. PERCENTAGE OF CHILDREN GIVING A NEGATIVE SCHICK TEST ACCORDING TO AGE, SEX, AND DOSE

6- 8 incl.	271	37	88.0	222	46	82.8	493	83	85.6
9-11 incl.	105	26	80.1	103	39	72.5	208	65	76.1
12	40	13	75.5	41	14	74.5	81	27	75.0
Total	416	76	84.5	366	99	78.7	782	175	81.7

and the ability to give a negative Schick reaction after the administration of toxoid. Both Tables IA and IB demonstrate that the percentage of negative reactions is higher among males than among females. These figures are proved to be of statistical significance. These findings are contrary to what Benjamin and his co-workers found in their studies.

Both Tables IA and IB show that the group of children immunized at six months of age gave a greater percentage of Schick-negatives than those immunized at nine months or one year of age. This result is shown

in Table IA, where the percentage of negatives at 6 months is 86.9, while at 12 months it is 75 per cent. The fact that there is a higher percentage of negatives at 6 months is not due to active immunity conferred by the toxoid immunization, but rather to the passive immunity inherited from the mother. These figures, though not highly so, are of statistical significance, and the association is not due to chance.

Tables IIA and IIB show time relationship between immunization and the Schick test. Table IIB is similar to Table IIA, the only exception being that the age groups are rearranged for simplification. Table IIB shows that the group of children Schick-tested six months after immunization give a higher percentage of negatives than when Schick-tested one year after immunization. Thus a group of 95 children, Schick-tested at six months after inoculation, show a percentage of 93.7 negative, while a similar group 133 children, immunized at the same age, but Schick-tested one year after, show a percentage of 79.7 negative, or a difference of 12.1 per cent. In other words, the percentage of positives in the first is 6.3 per cent while those in the second group show a percentage

TABLE II

RESULTS OF 2 DOSE TOXOID IMMUNIZATION IN CHILDREN 1 YEAR OR UNDER

A. PERCENTAGE OF CHILDREN GIVING A NEGATIVE REACTION ACCORDING TO TIME INTERVAL BETWEEN IMMUNIZATION AND SCHICK TEST

AGE IN MONTHS AT TIME OF IMMUNIZATION	4-6 MO. INCL.			7-11 MO. INCL.			1-1.9 YR. INCL.			2 YEAR & OVER		
	NEG.	POS.	% NEG.	NEG.	POS.	% NEG.	NEG.	POS.	% NEG.	NEG.	POS.	% NEG.
6	42	4	91.3	108	16	87.1	38	4	90.5	11	6	64.7
7	30	1	96.8	91	14	86.7	33	9	78.6	9	3	75.0
8	17	1	94.4	70	5	93.3	35	14	71.4	9	6	60.0
9	12	0	100	39	13	75.0	31	5	86.1	8	7	53.3
10	7	1	87.5	31	6	83.8	24	8	75.0	2	4	33.3
11	5	1	83.3	22	3	88.0	19	7	73.1	8	10	44.4
12	15	2	88.2	25	8	75.8	29	8	78.4	12	9	57.1
Total	128	10	92.8	386	65	85.6	209	55	79.2	59	45	56.7

B. PERCENTAGE OF CHILDREN GIVING A NEGATIVE REACTION ACCORDING TO TIME INTERVAL BETWEEN IMMUNIZATION AND SCHICK TEST

6-8	89	6	93.7	269	35	88.5	106	27	79.7	29	15	65.9
9-11	24	2	92.3	92	22	80.7	74	20	78.7	18	21	46.1
12	15	2	88.2	25	8	95.8	29	8	78.4	12	9	57.1
Total	128	10	92.8	386	65	85.6	209	55	79.2	59	45	56.7

of 20.3 positive, which is three times as much as the first group. Almost the same percentage is obtained, regardless of the age of immunization. It is evident then from these figures, which are of statistical significance, that infants Schick-tested one year after immunization instead of after six months will more likely present a better gauge as to the degree of immunity conferred. It may be explained in Tables IIA and IIB that

while there is some indication that some children were Schick-tested between 4 and 6 months and between 1 and 2 years of age, the number of children under 6 months and over 1 year of age were relatively few.

Tables IIIA and B and IVA and B show a group of children immunized with one dose of alum toxoid. Tables IIIA and B show a group of children immunized by private physicians, while Tables IVA and B show a group of children immunized by school physicians. Although the number of children immunized here is small and is not of statistical significance, it shows, however, some interesting points. The first is that the figures show consistently a higher percentage of negatives, regardless of age at time of immunization. The second point of interest is that, of the group of 95 children immunized by school physicians, 58 were Schick-tested again from two to three years after immunization. Seven of this group were found to be positive, showing a reversal of 12.1 per cent. This percentage is much smaller than that shown when two doses of toxoid are given.

TABLE III

RESULTS OF ALUM TOXOID (1 DOSE) IN CHILDREN UNDER 5 YEARS (PRIVATE PHYSICIANS)

A. PERCENTAGE OF CHILDREN GIVING A NEGATIVE SCHICK TEST ACCORDING TO AGE, SEX, AND DOSE

AGE AT TIME OF IMMUNIZATION	MALES			FEMALES			BOTH SEXES		
	NEG.	POS.	% NEG.	NEG.	POS.	% NEG.	NEG.	POS.	% NEG.
Under 6 mo.	1	0	100	1	0	100	2	0	100
6-8 mo. incl.	27	2	93.1	17	1	94.4	44	3	93.6
9-11 mo. incl.	10	1	90.9	6	1	85.7	16	2	88.9
1-1.9 yr. incl.	8	0	100	7	0	100	15	0	100
2-5 yr. incl.	3	3	50.0	3	1	75.0	6	4	60.0
Total	49	6	89.1	34	3	91.9	83	9	90.2

B. RELATION OF CHILDREN GIVING A NEGATIVE REACTION ACCORDING TO TIME INTERVAL BETWEEN IMMUNIZATION AND SCHICK TEST

AGE AT TIME OF IMMUNIZATION	2-6 MO. INCL.			7-11 MO. INCL.			1-1.9 YR. INCL.			2 YR. & OVER		
	NEG.	POS.	% NEG.	NEG.	POS.	% NEG.	NEG.	POS.	% NEG.	NEG.	POS.	% NEG.
Under 6 mo.	1	0	100	1	0	100	0	0	00.0	0	0	00.0
6-8 mo. incl.	17	2	89.5	17	0	100	7	0	100	3	1	75.0
9-11 mo. incl.	6	0	100	6	0	100	3	1	75.0	1	1	50.0
1-1.9 yr. incl.	6	0	100	1	0	100	7	0	100	1	0	100
2-5 yr. incl.	1	0	100	2	0	100	3	4	42.9	0	0	00.0
Total	31	2	93.9	27	0	100	20	5	80.0	5	2	71.4

Table V illustrates results for a group of children who have been immunized and have been found to be negative after the first Schick test. These children were then Schick-tested again to determine the percentage of reversals As this table indicates, these children were Schick-tested again from one to five years after they were first Schick-tested and found to be negative. Of a total of 180 children, there were 134 negative and

TABLE IV

RESULTS OF ALUM TOXOID (1 DOSE) IN CHILDREN UNDER 5 YEARS (SCHOOL PHYSICIANS)

A. PERCENTAGE OF CHILDREN GIVING A NEGATIVE SCHICK TEST ACCORDING TO AGE, SEX, AND DOSE

AGE AT TIME OF IMMUNIZATION	MALES			FEMALES			BOTH SEXES		
	NEG.	POS.	% NEG.	NEG.	POS.	% NEG.	NEG.	POS.	% NEG.
6-8 mo. incl.	16	0	100	13	0	100	29	0	100
9-11 mo. incl.	10	0	100	4	0	100	14	0	100
1-1.9 yr. incl.	17	0	100	9	0	100	26	0	100
2-5 yr. incl.	13	0	100	13	0	100	26	0	100
Total	56	0	100	39	0	100	95	0	100

B. RELATION OF CHILDREN GIVING A NEGATIVE REACTION ACCORDING TO TIME INTERVAL BETWEEN IMMUNIZATION AND SCHICK TEST

AGE AT TIME OF IMMUNIZATION	2-6 MO. INCL.			7-11 MO. INCL.			1-1.9 YR. INCL.			2 YR. & OVER		
	NEG.	POS.	% NEG.	NEG.	POS.	% NEG.	NEG.	POS.	% NEG.	NEG.	POS.	% NEG.
6-8 mo. incl.	25	0	100	4	0	100	0	0	00.0	0	0	00.0
9-11 mo. incl.	14	0	100	0	0	100	0	0	00.0	0	0	00.0
1-1.9 yr. incl.	23	0	100	3	0	100	0	0	00.0	0	0	00.0
2-5 yr. incl.	25	0	100	1	0	100	0	0	00.0	0	0	00.0
Total	87	0	100	8	0	100	0	0	00.0	0	0	00.0

46 positive, or a reversal of 25.5 per cent. Although this group presents a very small number and is not of statistical significance, it brings out several interesting points:

1. That the percentage of reversals out of the entire group is 25.5.

2. That the highest percentage of reversals appears to be in children who were immunized between six and nine months of age.

3. That the greatest number of children became positive again between two and four years after immunization (70 per cent).

It appears then from Table V that the children immunized at an early age are protected against diphtheria for a period of no longer

TABLE V

DATA CONCERNING 180 CHILDREN WHO HAD BEEN SCHICK-TESTED AGAIN AFTER HAVING BEEN ONCE NEGATIVE TO THE SCHICK REACTION

AGE AT TIME OF IMMUNIZATION	ELAPSED TIME BETWEEN SECOND SCHICK TEST AND IMMUNIZATION										TOTAL % POS.		
	1-1.9 YR.		2-2.9 YR.		3-3.9 YR.		4-4.9 YR.		5 YR. & OVER				
	NEG.	POS.	NEG.	POS.	NEG.	POS.	NEG.	POS.	NEG.	POS.	NEG.	POS.	% POS.
6 mo.	6	3	11	6	3	0	1	1	0	0	21	10	32.7
7-8 mo.	3	2	2	1	3	3	1	2	0	0	9	8	48.0
9-11 mo.	0	0	2	1	1	2	4	1	0	0	7	4	36.4
1-1.9 yr.	3	0	4	1	2	0	4	1	0	1	13	3	13.1
2-2.9 yr.	1	0	2	1	1	1	2	0	0	0	6	2	25.0
3-4.9 yr.	2	1	6	0	8	0	3	0	0	0	19	1	5.0
5 and over	7	0	21	6	21	9	9	3	1	0	59	18	23.3
Total	22	6	48	16	39	15	24	8	1	1	134	46	25.5

than four years. Thus it seems that in a community of this size, if children are to be immunized at that early age (under 9 months), it would be a sound public health procedure to Schick-test them again before entering school.

SUMMARY

1. This study indicates that there is a higher percentage of negative reactions in a group of children immunized between 6 and 9 months of age than when immunized at 1 year of age. The high percentage of negative reactions is probably not due to the immunity conferred as the result of toxoid administration, but is influenced to the passive immunity inherited from the mother. This confirms the results of studies made by other investigators. While toxoid immunization against diphtheria will add protection to a larger percentage of children if performed at a later age after the passive immunity derived from the mother is gone, this is no indication against immunization before 9 months of age, when a public health program is considered. But children must be Schick-tested after immunization and again Schick-tested at a later period of time if we are to be certain of results in individual cases. Immunization at a later age is more applicable where the private practitioner is concerned because the child is under closer observation and because there are other preventive measures which the private practitioner institutes at six months of age, such as whooping cough inoculation and vaccination against smallpox.

2. As regards time relationship between immunization and Schick test reaction, it was shown here that the percentage of negative reactions is considerably smaller when infants are Schick-tested one year after immunization than when Schick-tested six months after immunization. In other words, there is a decline in the ability to give a negative reaction as the time interval between the last dose of toxoid and the Schick test is prolonged. It seems, therefore, that it would be a safe and wise procedure to Schick-test children one year after immunization instead of six months. In this manner a better gauge may be obtained as to the degree of immunity conferred.

3. Concerning the problem of the reversal from Schick-negative to the Schick-positive, this study has shown that there is a 25 per cent reversal when children are immunized with two doses of toxoid. It also indicated that many became positive two or three years after immunization. This suggests the desirability of Schick-testing children again before they enter school.

4. Regarding the effectiveness of two doses of toxoid in comparison with three doses of toxoid, this study has shown that the percentage of negative reactions is much smaller when two doses are administered than when three doses are given. Thus our analysis shows that when two doses are administered, the percentage of Schick negatives is 81.7

per cent while, when three doses are administered, the percentage is about 96 per cent as shown by Benjamin and his co-workers. We have also shown here that one dose of alum-precipitated toxoid is more effective than two doses of the liquid toxoid. It would seem, therefore, that three doses of unmodified toxoid given at four-week intervals is the most effective method of diphtheria immunization.

5. In regard to Schick testing after immunization—while it may not be good economy in larger cities, in communities like New Haven, it is a necessary procedure. We differ with Benjamin when he states that it is unnecessary to make Schick tests before and after immunization. The result of this study indicates that the Schick test after immunization is a necessary public health procedure.

CONCLUSIONS

1. It appears that sex may be a factor or that a definite relationship exists between sex and the ability to give a negative Schick reaction after the administration of toxoid.

2. The number of Schick-negatives is much greater in infants immunized at 6 months of age than in those immunized at 1 year of age. This does not imply that it is advisable to immunize at an early age.

3. A definite decline is noted in the ability to give a negative Schick reaction when infants are Schick-tested one year after immunization rather than at six months after immunization.

4. The percentage of reversals as the result of two-dose toxoid administration in this study was 25.5 per cent and 70 per cent of these reversals occurred between two and four years after immunization.

5. This study confirms the opinion of the other investigators that three doses of toxoid are superior to two doses of toxoid.

REFERENCES

1. Maloney, P. J., and Fraser, C. J.: Am. J. Pub. Health **17:** 1027, 1927.
2. Greengard, J.: Am. J. Dis. Child. **47:** 799, 1934.
3. McKahnn, C. P., and Kapnick, I.: J. PEDIAT. **13:** 907, 1938.
4. Park, W. H., cited by Blum, Julius: J. A. M. A. **98:** 1627, 1929.
5. Greengard, Joseph: Arch. Pediat. **49:** 526, 1932.
6. Greengard, J., and Bernstein, H.: J. A. M. A. **105:** 341, 1935.
7. Benjamin, B., Fleming, G., and Ross, M. A.: Am. J. Dis. Child. **55:** 51, 1938.
8. Blum, Julius: J. A. M. A. **98:** 1627, 1929.
9. Ramon, G., and Debré, R.: Cited by Provitsky, O. R.: Am. J. Pub. Health **22:** 29, 1932.
10. Fitzgerald, J. G., Fraser, D. I., McKinnon, N. E., and Ross, M. A.: New York Acad. Med. **14:** 566, 1938.

TREATMENT OF CRYPTORCHIDISM WITH MALE SEX HORMONE

CARL ZELSON, M.D., AND ERNST STEINITZ, M.D.
NEW YORK, N. Y.

SINCE the reports of Aschheim and Zondek (1926)[1] on the effects of pregnancy urine on the sex organ and of Engle (1932)[2] on the effects of gonadotropic hormone in causing descent of testes in immature monkeys, many reports have appeared showing the beneficial effect of this hormone in human cryptorchidism. In a recent publication, Zelson[3] has summarized the literature to date and has shown that in a carefully selected group of children with cryptorchidism treated with gonadotropic hormone he could bring about the descent of the testicles in 31 per cent of the cases. Though earlier publications reported success in about 61 per cent, some of the later reports concur with Zelson's lower percentage of successful results.

It is certainly desirable to improve, if possible, on the results heretofore obtained. As we know that the gonadotropic hormone stimulates the interstitial cells of the testicle which produce the male sex hormone, there arises the question whether its action in cryptorchidism is wholly or partly effected through stimulation of the production of the male sex hormone. Assuming the affirmative, one could expect to obtain improved results by direct application of the male sex hormone, whether alone or in conjunction with the gonadotropic hormone.

Comparatively little work has thus far been done on the use of male sex hormone in cryptorchidism. Mention will later be made of the few experiments conducted with the older male sex hormone preparations. During the last decade or so remarkable progress has been made in the knowledge concerning male sex hormones. McGee[4] was the first to obtain a male sex hormone from the testes and to prove its androgenic properties by its influence on the growth of the capon comb. Loewe and Voss,[5] Gallagher and Koch,[6] Funk and Harrow,[7] and others were able to extract an androgenic substance of testicular origin from male human urine. Butenandt and his associate[8, 9] were the first to obtain the hormone in crystalline form from the urine and to find its chemical and also its structural formula. They called the hormone "androsterone." This substance, extracted from the male human urine, was considered to be the male sex hormone proper, identical with the hormone obtained from the testes. But Gallagher and Koch[10] extracted from testes a substance about ten times more potent, and somewhat different chemically, as evidenced by the fact that the testicular extract was destroyed on boiling

From the Pediatric Service of Dr. Bela Schick, Mount Sinai Hospital.

with alkali, while the urinary extract was not affected by like treatment. However, they believed both substances to be biologically identical, attributing the greater potency of the testicular hormone to greater purity. Laqueur and his coworkers[11, 12, 13, 14] extracted from the testes a crystalline substance of the same potency as the Gallagher and Koch testis extract. They proved it to be biologically different from androsterone. It was not only very effective in producing growth of the capon comb, but was also effective in bringing about complete restitution of secondary sex characteristics. This second effect could not be obtained by means of the hormone extracted from the urine. They also found its chemical formula to be different from that of androsterone in that a double bond was present, and therefore two hydrogen atoms less, and also that the keto group was in a different position. They called the new hormone "testosterone." About the same time, Ruzicka and Tschopp[15] and Butenandt and his group,[16, 17] starting with cholesterol, succeeded in synthesizing a hormone which proved by its chemical and biologic properties to be identical with testosterone. They also confirmed the chemical structural formula as suggested by Laqueur. Testosterone, therefore, is now generally considered to be the male sex hormone proper.

In addition to testosterone, Laqueur's group extracted from testes some unknown substances which in themselves had no effect on the genitals, but which accentuated the effect of testosterone, but not of androsterone, again proving that the two substances were not identical. Increased activity of testosterone was also found to result from esterification with organic acids, like acetic or propionic acid, as reported by Miescher, Wettstein, and Tschopp.[18] Testosterone propionate, therefore, is the form in which the male sex hormone is now generally used in therapeutics.

This powerful new hormone proved to be effective in inducing descent of testes in animal experiments. Hamilton,[19] in 1936, using 5 mg. of testosterone propionate several times weekly, caused the descent of the testes in nine immature male macaques (in which cryptorchidism exists until puberty). He was able to obtain descent in all cases after fourteen days, and he felt that this was due to the growth of the cord and development of the scrotum.

Denk and Uebelhoer[20] were the first to attempt to treat cryptorchidism in the human with male sex hormone. They used a preparation administered orally called "testosan." This was used alone, in combination with pituitary extract, orally and rectally, or in combination with injections of anterior pituitary-like hormone. They reported very favorable results. Of the 19 patients treated, 6 showed complete descent of the testicles, and 9 showed a partial effect. Those patients whom the testicles had not been found previously but were felt in the canals after the treatment were considered as improved. These amazing results are puzzling. It seems hard to conceive that an oral medication given

in the dosage described could be so potent as to cause descent of the testicles in a comparatively short period of time. Most endocrine products given orally, even when potent, must be given in very large doses to obtain results.

Sand[21] reported the successful treatment of one case of cryptorchidism with the use of a Danish androsterone preparation in combination with a gonadotropic hormone.

Bize[22] was the first to try the new hormone testosterone. He gave 10 mg. of testosterone propionate every five days to boys with cryptorchidism, without any effect. He does not state how many cases were treated or how long treatment was continued. Zeithaml[23] used testosterone propionate in a controlled series of cryptorchid children. He treated eight boys between 4½ and 15 years of age by giving them from 10 to 30 mg. weekly, totaling between 17.5 and 145 mg. The hormone did not produce descent of the testicles in any of his patients. Bruce Webster[24] gave 25 mg. of the testosterone propionate three times a week for several months to two boys aged 10 and 14 years, respectively, with no result. Hamilton and Hubert[25] gave from 5 to 20 mg. of the preparation, three to seven times a week, to seventeen boys between the ages of 1½ and 27 years, for a period as long as five months in some cases. They obtained descent in one of nine unilateral cases and in three of eight bilateral cases. In each of two bilateral cases one testicle descended into the scrotum, while the other remained undescended. Partial descent occurred in two of the bilateral cases.

We are herewith presenting a report on a group of cryptorchid children treated with male sex hormone, from which an evaluation of its effectiveness may be made. Though our results are not startling, we feel that the effect of the treatment as given to a group of children chosen under very strict criteria is of sufficient interest to warrant a report.

CHOICE OF CASES

All the cases treated in this series were from the Children's Out-Patient Department of the Mount Sinai Hospital, New York. There were 20 children between the ages of 7½ and 13 years. Most of these children had been seen at intervals from a period of three to six months before treatment was instituted. Eleven of the 20 children had had previous treatment with gonadotropic hormone, the amounts varying between 5,100 and 40,000 units. Each boy selected for treatment satisfied the following rigid criteria given by Zelson:[3]

1. Each boy was examined both in standing and reclining positions by at least two physicians who had to be unanimous in the diagnosis.
2. At no time in the past history of the children had the undescended testicle been seen or felt in the scrotum.
3. Testicles could not be pulled or forced into the scrotum.

4. Testicles could not be brought down into the scrotum after twenty to thirty minutes under a heat lamp or after a warm bath.

If, in spite of the above criteria, descent occurred after one, two, or three injections, the case was not included in our series. We feel that in this type of case the testicles would descend spontaneously.

Seventeen cases were unilateral, and 3 were bilateral. In 7 of the 17 unilateral cases, the testicles could not be felt at any time; in the remaining 10 cases, the testicle was at various levels in the canal. In each of the bilateral cases one testicle was in the canal, and the other testicle could not be felt. There was a total of 23 undescended testicles; 13 were palpable, and 10 were not.

TREATMENT

Each child was treated with testosterone propionate. The testosterone propionate used was the synthetic product manufactured by the Roche-Organon Co. under the trade name of neo-hombreol. The strength of the product used by us was 10 mg. per cubic centimeter. Each boy was given three injections a week over a period of from four to ten weeks; the doses varied between 5 and 10 mg. an injection. The total dosage varied between 60 and 180 mg. Four of the boys who had received a series of testosterone propionate injections for from four to seven weeks were given a second series of injections of testosterone propionate, 5 mg., three times a week, in combination with gonadotropic hormone (pregnyl), 500 units, three times a week, for a period extending over three to six weeks.* The four children who were given the combined treatment received, in addition to the testosterone propionate, a total dosage of gonadotropic hormone varying between 4,000 and 8,900 units. None of the children received treatment longer than ten weeks.

RESULTS

Twenty boys with twenty-three undescended testicles were treated with testosterone propionate (Table I). In 17 of these boys the condition was unilateral; in 3 of the boys it was bilateral. Eleven of the boys had been previously treated with gonadotropic hormone with no effect. Of these 11 boys, 2 responded to the testosterone treatment: one was a unilateral case, and the other a bilateral case; both were pseudo-Froehlich types. There was complete descent in 3 cases, i.e., 15 per cent of the entire group. Of these 3, 1 had unilateral cryptorchidism, and 2, bilateral. That the testosterone propionate had a partial effect on some of the other children treated is evident by the following facts: In 5 cases the testicles came down to the lower end of the canal and could be

*The authors gratefully acknowledge the cooperation of Dr. Louis Klein of the Roche-Organon Company in supplying neo-hombreol and pregnyl for this clinical investigation.

TABLE

CASE NO.	AGE	UNDESCENDED TESTICLES		GENERAL APPEARANCE	PREVIOUS TREATMENT	DRUG USED	AMOUNT PER DOSE GIVEN	LENGTH OF TREATMENT
		SINGLE	BILATERAL					
1	9	Left in abdomen.		Obese.	8 mo. with A. P. L. substance at another institution with no result.	Test. prop.	5 mg. 3 × wk.	4 wk.
2	10	Rt. in canal.		Normal.	10,000 U. follutein with no result.	Test. prop.	10 mg. 3 × wk.	8 wk.
3	10	Left in canal.		Normal.	Given A. P. L. substance for a prolonged period with no result.	Test. prop.	10 mg. 3 × wk.	4 wk.
4	11	Rt. in abdomen.		Small for age.	5100 U. A. P. L. substance with no result.	Test. prop.	10 mg. 3 × wk.	4 wk.
5	11		Left in canal. Rt. in abdomen.	Small for age.	7750 U. follutein with no result.	Test. prop.	10 mg. 3 × wk.	5 wk.
6	10	Rt. in abdomen.		Froehlich type.	Antuitrin-S 3×wk. for 6 mo. No result.	Test. prop.	5-10 mg. 3 × wk.	9 wk.
7	11	Rt. in abdomen.		Normal.	15,000 U. follutein with no result.	Test. prop.	10 mg. 3 × wk.	6 wk.
8	11½	Rt. in canal.		Tall for age.	10,000 U. follutein with no result.	Test. prop.	5 mg. 3 × wk.	5 wk.
9	12	Left in canal.		Small for age.	10,000 U. follutein with no result.	Test. prop.	10 mg. 3 × wk.	4 wk.
10	13	Rt. at lower end of canal.		Small for age.	15,000 U. follutein with no result.	Test. prop.	10 mg. 3 × wk.	6 wk.
11	13		Left in canal. Rt. in abdomen.	Froehlich type.	40,000 U. follutein with no result.	Test. prop.	10 mg. 3 × wk.	8 wk.
12	7½	Rt. in canal.		Normal.	None.	Test. prop. Test. prop. plus pregnyl.	5 mg. 3 × wk. 5 mg. 3 × wk. 500 U. 3 × wk.	4 wk. 6 wk.

I

DOSAGE		PREGNYL	RESULTS				REMARKS
	TOTAL		GROWTH	GENERAL	SIZE OF TESTICLE	ON CRYPTORCHIDISM	
70 mg.			No change.	No change.	No change.	No change.	Left sided hernia. Was referred for repair of hernia.
200 mg.			No change.	Penis larger. Pubic hair.	Smaller.	No change.	Testicle was smaller, at end of canal, and could be pulled into the upper part of the scrotum.
120 mg.			No change.	Penis larger.	No change.	No change.	
120 mg.			Grew ½" in four weeks.	Penis larger.	Small; palpable in canal.	No change.	Testicle became palpable in canal.
160 mg.			No change.	Penis larger. Pubic hair.	Small.	No change.	Rt. testicle felt at lower end of canal. Left testicle in canal as before.
160 mg.			No change.	Penis and scrotum larger. Pubic hair.	No change.	Descent of testicle into upper part of scrotum.	Mother stated that "child acts more like a boy now."
170 mg.			No change	Penis larger. Pubic hair. Scrotum larger.	No change.	No change.	
75 mg.			No change	Penis larger. Pubic hair.	Smaller.	No change.	Rt. testicle became smaller and could be pushed out of canal.
120 mg.			No change.	Penis larger. Pubic hair.	Smaller.	No change.	
180 mg.			No change.	Penis larger. Pubic hair increased.	Smaller.	No change.	Testicle can be pushed out of canal.
200 mg.			No change.	Penis and scrotum larger. Much pubic hair.	Smaller.	Descent of both testicles into scrotum.	Was under thyroid medication for control of excessive weight.
60 mg. 85 mg.	145 mg.	7700	No change.	Penis larger. Scrotum larger.	No change.	No change.	Pregnyl was given in combination with testosterone in later half of treatment with no effect.

TABLE

CASE NO.	AGE	UNDESCENDED TESTICLES		GENERAL APPEARANCE	PREVIOUS TREATMENT	DRUG USED	AMOUNT PER DOSE GIVEN	LENGTH OF TREATMENT
		SINGLE	BILATERAL					
13	8	Rt. in abdomen.		Obese.	None.	Test. prop. Test. prop. plus pregnyl.	5 mg. 3 × wk. 5 mg. 3 × wk. 500 U. 3 × wk.	5 wk. 5 wk.
14	9	Rt. in abdomen.		Froehlich type.	None.	Test. prop. Test. prop. plus pregnyl.	5 mg. 3 × wk. 5 mg. 3 × wk. 500 U. 3 × wk.	7 wk. 3 wk.
15	10	Rt. in canal.		Normal.	None.	Test prop.	10 mg. 3 × wk.	4 wk.
16	10	Rt. in abdomen.		Obese. Small genitals.	None.	Test. prop.	5 mg. 3 × wk.	6 wk.
17	10½		Left in abdomen. Rt. in canal.	Normal.	None.	Test. prop.	10 mg. 3 × wk.	7 wk.
18	11	Left in canal.		Normal.	None.	Test. prop. Test. prop. plus pregnyl.	5 mg. 3 × wk. 5 mg. 3 × wk. 500 U. 3 × wk.	4 wk. 6 wk.
19	11	Rt. in canal.		Normal.	None.	Test. prop.	5 mg. 3 × wk.	4 wk.
20	11½	Left in canal, small.		Normal.	None.	Test. prop.	10 mg. 3 × wk.	4 wk.

pulled out of the external ring manually but retracted immediately when left alone. In 4 cases in which the testicles were not palpable at the onset of the treatment, they became palpable in the canal at the end of treament. There was enlargement of the penis in 16 cases, enlargement of the scrotum in 8 cases, and a definite growth of pubic hair in 10 cases. Only 4 of the boys showed no effect from the hormone. In 5 cases the testicles became smaller during the course of treatment. In one case the testicles became larger. In a four-week period one boy grew ½ inch in

1—Cont'd

DOSAGE		PREGNYL	RESULTS				REMARKS
	TOTAL		GROWTH	GENERAL	SIZE OF TESTICLE	ON CRYPTORCHIDISM	
70 mg. 70 mg.	140 mg.	5600	No change.	Penis larger. Penis and scrotum larger.	No change.	No change. Both testicles descended into scrotum.	Rt. testicle palpable. With test. alone no descent.
110 mg. 40 mg.	150 mg.	4000	No change.	Penis and scrotum larger. Pubic hair.	No change.	Rt. in canal and could be pulled into scrotum.	Combination of testosterone and pregnyl caused descent of the testes into scrotum.
120 mg.			No change.	No change.	No change.	No change.	
90 mg.			No change.	Penis larger.	No change.	Both in scrotum.	4 months after cessation of treatment penis was smaller but testicles remained in scrotum.
160 mg.			No change.	Penis and scrotum larger. Pubic hair.	No change.	Both palpable in lower end of canal.	After testosterone he was treated with 10,000 U. of pregnyl and both testicles descended into scrotum.
60 mg. 110 mg.	170 mg.	8900	No change.	Penis and scrotum larger.	No change. Left testicle larger.	No change.	No change other than enlargement of testicle in canal with combined treatment.
60 mg.			No change.	No change.	No change.	No change.	Did not continue treatment.
120 mg.			Grew 1" in four weeks.	No change.	No change.	No change.	Testicle at lower end of canal—can be pulled into scrotum.

height, and another grew 1 inch. Though frequent erections were reported during the course of treatment, there was no discomfort and no history of masturbation.

Four of the children who had not responded to the testosterone propionate alone were given a second course of treatment in which testosterone propionate was combined with gonadotropic hormone (pregnyl). All of these children had unilateral undescended testicles. Two of the 4 boys responded to this treatment with complete descent

of the testicle into the scrotum. One boy with bilateral cryptorchidism, in whom testosterone propionate was not effective, was subsequently given 10,000 units of gonadotropic hormone, with resultant complete descent of the testicles.

DISCUSSION

A large number of experiments have proved male sex hormone to be effective in promoting the growth of the genital organs in immature animals and in restoring secondary sex characteristics in castrated animals. Clinical experience has also confirmed the assumption that this hormone is essential for the maintenance of normal function in the male. It has been used a great deal in human hypogonadism and has caused reactivation of the sexual function and the libido, with enlargement of the penis, scrotum, and epididymis. It is of definite value in the treatment of impotence or of neurasthenic vasomotor troubles that appear at the male climacteric.

We believe that factors other than gonadotropic hormone are involved in the descent of the testicles. One must suppose that in cases of unilateral cryptorchidism, since one testicle is down, sufficient hormone must have been present to cause its descent. If no obstruction to the other testicle is present, it may inherently be abnormal so that it would not respond to the hormone present in the circulation. Whether the abnormality is anatomical or physiologic cannot be decided at present. It has been the opinion of most workers that the gonadotropic hormone acts on the interstitial cells of the testicles causing an increased secretion of the male sex hormone which in turn stimulates the development of secondary sex characteristics and descent of the undescended testicles. Others are of the opinion that the descent of the testicles is the result of a direct effect of the gonadotropic hormone. Hamilton[19] feels that testosterone propionate has a distinct advantage over gonadotropic hormone, the former being a pure synthetic drug which is stable and produces less widespread endocrine effects throughout the body. Furthermore, since he is of the opinion that the testicular descent obtained with gonadotropic hormone is due to a stimulation of the male sex hormone production, he did not have to depend on the presence of a normal functioning or anatomically normal testicle.

That there is a relationship between the pituitary gland and the testes and scrotum has been proved conclusively. Cutuly and his coworkers[26] have shown recently that, following hypophysectomy, testes will ascend into the canals. Male sex hormone injections tend to prevent this ascent of the testes into the canal with the subsequent degeneration of the testes and scrotum. In addition, Hamilton and Leonard[27] have shown that male sex hormone has a direct effect on the testes, as seen in changes produced by male substance on cryptorchid testes of hypophysectomized rats. These reports tend to substantiate our ideas on the

subject. However, our results have not borne out our hypothesis. Of course, it can be claimed that the dosage we used was comparatively small, and yet we feel that, since 16 of the 20 boys showed definite clinical effects, the dosage on the whole was adequate. It is interesting to note that the bilateral cases with a general endocrine imbalance responded most readily to the hormone. It would seem, therefore, that in these cases there is an inadequate secretion of pituitary gonadotropic hormone and, therefore, no male sex hormone secretion to cause the descent of the testicles. Replacement therapy is thus effective. As stated before, a normal testicle responds adequately, descending into the scrotum under stimulation of the gonadotropic hormone normally present in the blood stream. The abnormal testicle, if this is the cause of unilateral cryptorchidism, does not respond normally and remains in the canal or abdomen. If testosterone propionate is the final factor in the descent of normal testicles, the introduction of this factor should cause a descent of the undescended testicle, unless a mechanical obstruction is present. It seems hardly likely that such an obstruction is a major factor, since it seems to us that obstruction would not be present in as many children as failed to respond to treatment. We feel that for the normal descent of the testicles there must be present both a sufficient amount of gonadotropic hormone in the blood stream and a normally functioning testicle for the production of male sex hormone. The possibility that both elements are inadequate in cryptorchidism must be considered. If the testicular underfunction is slight, the injection of gonadotropic hormone may be sufficient to stimulate the testicle and produce descent. Such seems to be the case in a comparatively large number of instances. If, however, the testicular underfunction is more marked, additional supply of testicular hormone will be needed to produce descent. This effect was seen in two of our patients who had not responded to gonadotropic hormone but did respond to male sex hormone.

It must be remembered that the male sex hormone is not a complete substitute for an inadequate supply of gonadotropic hormone. The effects of both the gonadotropic hormone and the male sex hormone, though intimately related, are certainly not identical. It is frequently reported, and to some extent substantiated by our work, that with male sex hormone there is a decrease in the size of the testicles. The testicles in 5 of our patients became definitely smaller during treatment. Gonadotropic hormone, on the other hand, will enlarge the testicle.

The reports in the literature on the treatment of cryptorchidism with male sex hormone record many partial successes (Table II). Just what is meant by the expression is not stated definitely. Our partial successes, however, consist of those cases in which the testicles which were not palpable before treatment became palpable in the canal after treatment. It is our impression that these children will respond to further treatment

TABLE II

AUTHOR, YEAR	NO. OF CASES	AGES (YR.)	NO. OF CASES WITH UNDESCENDED TESTES		SUBSTANCE GIVEN	DOSE	LENGTH OF TREATMENT	SUCCESSFUL RESULTS			
								UNILATERAL		BILATERAL	
			UNILATERAL	BILATERAL				COMPLETE	PARTIAL	COMPLETE	PARTIAL
Denk and Uebelhoer (1936)	9	8-13	5	4	Testosan by mouth	6-8 tb. a day	5 wk. to 1 yr.	3	1	1	2
	10	5-12	5	5	Testosan orally and pituitary by mouth and by rectum. Testosan plus pregnyl	200-500 tb. 40-60 tb. 20-60 supp. 10-16 inj.			3	2	3
Sand (1937)	1	10		1	Danish andrin and Danish gonadotr. hormone	1000 cock U. 5700 mouse U.				1	
Bize (1937)	?	?	?	?	Testost. prop.	10 mg. every 5 days		0		0	
Zeithaml (1938)	8	4½-15	6	2	Testost. prop.	5 mg. 2 × wk. 10 mg. 3 × wk.	?	0		0	
Bruce Webster (1938)	2	10-14	1	1	Testost. prop.	25 mg. 3 × wk.	Several months	0		0	
Hamilton and Hubert (1938)	17	1½-27	9	8	Testost. prop.	5-20 mg. 3-7 × wk.	Up to 5 mo.	1		3	4
Total	47		26	21				4	4	7	9

with gonadotropic hormone. We were able to carry on this treatment in three of the boys and were successful in each case. (To be reported.)

We feel that at present the gonadotropic hormone should still be the hormone of choice for treatment of cryptorchidism. In some cases the most desirable type of therapy should be a combination of both hormones, particularly in those which do not respond to gonadotropic hormone alone.

SUMMARY

1. A review of the 47 cases in the literature on the treatment of cryptorchidism with male sex hormone is presented in tabular form. Eleven (23.4 per cent) of the cases responded to treatment with complete descent of the testicles; and 13 (27.6 per cent) of the cases showed only a partial response to therapy.

2. Twenty boys with cryptorchidism were treated with male sex hormone: 17 of the boys had unilateral undescended testicles, and 3 of the boys had bilateral undescended testicles.

3. Three (15 per cent) of the cases responded to therapy with complete descent of the testes; one was a unilateral case, and two were bilateral.

4. Partial effect was obtained in 9 (45 per cent) of the cases treated. In these cases the testicles which had not been palpable before treatment became palpable after treatment and could be pulled into the scrotum. In 4 of the cases where the testicles were palpable at the onset of treatment, there was an apparent lengthening of the cord so that the testicles could be pulled into the scrotum.

5. Further treatment with gonadotropic hormone should be instituted in those children who show a partial response to the male sex hormone.

6. Male sex hormone seems to be the most effective in those bilateral cases which show some endocrine disturbance.

7. Though male sex hormone will produce an enlargement of the penis and scrotum and growth of pubic hair, it has a marked tendency to cause a shrinkage in the size of the testicle, both descended and undescended.

8. Gonadotropic hormone is more effective than male sex hormone in the treatment of cryptorchidism. However, some cases which do not respond to gonadotropic hormone alone will respond to therapy when given a combination of gonadotropic and male sex hormone.

REFERENCES

1. Aschheim, S., and Zondek, B.: Ztschr. f. Geburtsh. u. Gynäk. **90**: 372, 1926.
2. Engle, E. T.: Endocrinology **16**: 513, 1932.
3. Zelson, C.: J. Pediat. **14**: 452, 1939.
4. McGee, L. C.: Proc. Int. Med., Chicago **6**: 242, 1927.
5. Loewe, S., and Voss, H. E.: Acad. Anzeigen, 1929.
6. Gallagher, T. F., and Koch, F. C.: II Internat. Congr. Sex Research, London, 1930, pp. 312 and 322.

7. Funk, C., and Harrow, B.: Proc. Soc. Exper. Biol. & Med. **26**: 325 and 569, 1929.
8. Butenandt, A.: Ztschr. f. ang. Chem. **44**: 905, 1931.
9. Butenandt, A., and Tscherning, K.: Ztschr. f. physiol. Chem. **229**: 167, and 185, 1934.
10. Gallagher, T. F., and Koch, F. C.: Endocrinology **18**: 107, 1934.
11. Freud, J.: Proc. II. Internat. Congr. Sex Research, London, p. 304, 1930.
12. David, K., Dingemanse, E., and Polak, J. J.: Arch. internat. de pharmacol. et de thérap. **57**: 369, 1937.
13. Freud, J., Dingemanse, E., Freud, J., and Laqueur, E.: Ztschr. f. physiol. Chem. **233**: 281, 1935.
14. Freud, J., and Laqueur, E.: Act. brev. Neerl. physiol. **4**: 100, 1934.
15. Ruzicka, L., and Tschopp, E.: Schweiz. med. Wchnschr. **64**: 1118, 1934.
16. Butenandt, A., and Hanisch, G.: Ztschr. f. physiol. Chem. **237**: 89, 1935.
17. Butenandt, A., and Dannenbaum, H.: Ztschr. f. physiol. Chem. **229**: 192, 1934.
18. Miescher, K., Wettstein, A., and Tschopp, E.: Schweiz. med. Wchnschr. **36**: 763, 1936.
19. Hamilton, J. B.: Am. J. Physiol. **119**: 325, 1937.
20. Denk, W., and Uebelhoer, R.: J. internat. de chir. **1**: 369, 1936.
21. Sand, Knud: Endokrinologie **19**: 306, 1937.
22. Bize, P. R.: Bull. Med., Paris **51**: 803, 1937.
23. Zeithaml, Carl E.: Clin. Bull. Univ. Hosp. of Cleveland **2**: 67, 1938.
24. Webster, Bruce: J. PEDIAT. **13**: 847, 1938.
25. Hamilton, J. B., and Hubert, C.: Proc. Soc. Exper. Biol. & Med. **39**: 4, 1938.
26. Cutuly, E., McCullagh, D. R., and Cutuly, E. C.: Am. J. Physiol. **119**: 121, 1937.
27. Hamilton, J. B., and Leonard, S. L.: Anatomical Record—in press.

498 WEST END AVENUE
667 MADISON AVENUE

TRAUMATIC RUPTURE OF THE SPLEEN IN CHILDREN

With Special Reference to Left Shoulder Pain

Nina A. Anderson, M.D.
Cincinnati, Ohio

TRAUMATIC rupture of the spleen has occurred in 10 children observed in the Cincinnati Children's Hospital, the Cincinnati General Hospital, and the Ohio Soldiers' and Sailors' Orphans' Home, Xenia, Ohio, during the past fifteen years. In the review of this group of patients, emphasis has been placed upon the symptomatology.

OBSERVATIONS

The ages of these 10 children ranged from 5 to 15 years, and all but 3 were boys. The injury was caused by an auto accident in 5 instances, by sled riding in 3, by a fall from a bicycle in 1, and by a fall on to railroad tracks in 1.

Symptoms.—The most common symptoms of splenic damage were abdominal pain and tenderness. Eight children complained of pain in the abdomen within a few hours after the accident, and all of the group developed localized tenderness, dullness in the flank, or some splinting of the regional muscles.

Pain in the left shoulder was an important symptom in 5 of the 10 children. In one instance this was such an outstanding symptom that the parents insisted that the shoulder, and not the abdomen, was the site of the injury. The pain in this locality is probably referred from the motor fibers of the phrenic nerve to the sensory fibers of the midcervical nerves distributed about the shoulder.

The symptoms of shock occurred with varying severity in several children. Signs of external injury and fractures of the ribs were infrequent. Vomiting, which has been observed by other clinicians, was not a symptom in any of the children in the present series.

Laboratory Procedures.—The progressive increase in the pulse rate, the decline in the systolic blood pressure reading, the decrease in the number of red blood cells, and the increase in the number of white blood cells (especially the polymorphonuclear cells) assisted in the diagnosis of internal hemorrhage.

Outcome.—Splenectomy was performed in 9 children. In every instance the organ had ruptured, and there was gross hemorrhage into the surrounding space. All but one of the spleens removed at operation were normal except for the traumatic lesions. In one speci-

From The Children's Hospital Research Foundation, Cincinnati, Ohio, and the Department of Pediatrics, College of Medicine, University of Cincinnati.

men, in addition to the acute hemorrhage, microscopic tubercles were discovered. The tuberculin test of this patient was negative and, when he was observed ten months later, there was no evidence of tuberculosis. Two children died postoperatively. In the tenth patient, who died before operation could be performed, necropsy showed that, in addition to the rupture of the spleen, there had been rupture and laceration of the liver and of the lower lobe of the right lung, fracture of the sixth rib on the right side, and hemorrhage into the right pleural cavity and the retropleural and the retroperitoneal spaces.

The following history is typical of traumatic rupture of the spleen in the children of our group.

CASE REPORT

On Dec. 10, 1937, a 15-year-old white boy who was sled riding in "belly-buster" fashion struck a pile of earth with considerable impact. He was brought to the hospital of the Ohio Soldiers' and Sailors' Orphans' Home complaining of pain in his abdomen and in his left shoulder. He preferred to sit upright. There were no symptoms of shock; the heart sounds were normal, and the pulse was of good quality. An area of erythema and a superficial abrasion could be seen in the region of the eleventh rib in the left mid-axillary line. Pain could be elicited by lateral compression of the left chest, but not by anteroposterior compression. There was tenderness in the left upper quadrant but none in the costophrenic angle nor along the left ribs. Neither the spleen nor any other abnormal mass could be palpated in the abdomen. No local injury could be detected in the left scapular area. There were no signs of pleural effusion.

Within a few hours the pain in the left upper quadrant increased in severity, the skin and mucous membranes became pale, and the boy became very thirsty. His pulse rate fluctuated between 72 and 90, the quality remaining good. The abdominal pain was relieved somewhat when he lay on his right side, although he had a dull ache in the right shoulder and the right diaphragmatic region when he was in this position. The pain in the left scapular area was greatly exaggerated by any change from this position. A fullness developed in the left flank, and a mass was palpated in this area. He was nauseated at the time of admission, but this symptom did not recur; there was no vomiting. He voided without pain, and the urinalysis was negative. He passed two normal stools without difficulty. During the period of observation the following changes were noted in the blood picture and in the blood pressure:

TIME	R.B.C	W.B.C.	DIFFERENTIAL		B.P.
			POLY.	LYMPH.	
2:30 P.M.	6,670,000	13,200	66%	34%	114/66
4:30 P.M.	4,600,000	16,650	88%	12%	90/56
6:30 P.M.	3,750,000	12,000	85%	15%	96/64

Five hours after admission, he was taken to the McClellan Hospital where a ruptured spleen weighing 250 gm. was removed.

REVIEW OF THE LITERATURE

More than 100 cases of traumatic rupture of the spleen in patients under 16 years of age have been reported in the medical literature dur-

ing the past two decades. Available data[2, 3, 8, 9, 10] regarding eighty of these children, together with the ten observed by us, have been analyzed.

Age and Sex Distribution.—The great majority of accidents of this type have occurred in children of school age and much more frequently in boys than in girls (Table I). An instance of traumatic rupture

TABLE I

AGE AND SEX DISTRIBUTION OF TRAUMATIC RUPTURE OF THE SPLEEN IN CHILDREN

AGE IN YR.	MALE	FEMALE	SEX NOT RECORDED	TOTAL
4	1	2		3
5	1			1
6	2	3		5
7	5	4		9
8	5	1	1	7
9	10	2	1	13
10	10	1		11
11	4	4		8
12	6	1		7
13	4	1		5
14	13			13
15	4	2	2	8
Total	65	21	4	90

of the spleen occurring in a newborn infant who had been dropped on the floor in a precipitate delivery was reported by Simpson and quoted by Robitshek,[2] but this case has not been included in this analysis.

Type of Injury.—The injury was sustained most frequently in an automobile accident. Among 37 patients injured by a moving vehicle, 24 had been run over by its wheel. Thirty-two of these children had fallen, only 7 from considerable heights. Direct blows to the abdomen were received in 13 cases. Projecting objects had inflicted severe body injuries in 9 patients, who had fallen while running, sledding, or bicycling. Crushing injuries occurred in 2 patients (Table II).

TABLE II

TYPE OF TRAUMA CAUSING RUPTURE OF THE SPLEEN IN 90 CHILDREN

TYPE OF TRAUMA	NUMBER OF PATIENTS	PERCENTAGE OF TOTAL
1. Injury by a moving vehicle	37	41
2. Fall	32	36
3. Direct blow	13	14
4. Sledding accident	6	7
5. Crushing force	2	2
Total	90	100

It has been reported frequently in the literature that a rapid blow to the left flank is more apt to cause splenic hemorrhage than a heavy blow, possibly because the abdominal muscles have not had time to exert any resistance.

Symptoms.—No symptoms were recorded for 5 patients. Among the remaining 85 children of this series, abdominal symptoms, including pain, muscle spasm, tenderness, and fullness in the flank, were reported in 82 patients. There was some degree of shock in 65, and vomiting occurred in 23 children.

Shoulder pain was noted in fifteen instances. Its cause could not be definitely attributed to splenic trauma in one child who had received a fracture of the humerus in the same accident. The association of shoulder pain with injuries about the diaphragm has sometimes been designated as Kehr's sign. Homans[1] stated that it is a usual complaint of patients with ruptured spleens. It occurred in 7.8 per cent of the series of such patients reported by Robitshek.[2] No mention of the symptom was made among the 20 patients observed by McCracken.[3] Brogsetter, quoted by Connors,[4] has emphasized the fact that it is not a diagnostic symptom of splenic rupture alone, since other abdominal injuries, especially trauma to the left lobe of the liver, may also produce shoulder pain.

Seventeen of the children in the series had sustained superficial abrasions. Eleven had associated fractures. Four had lacerations of some other viscus besides the spleen (Table III). In this group of 90 children, 72 splenectomies were performed, and a total of 73 children recovered.

TABLE III

RELATIVE FREQUENCY OF THE DIFFERENT RECORDED FINDINGS PRODUCED BY RUPTURE OF THE SPLEEN IN 85 CHILDREN

FINDINGS	NUMBER OF PATIENTS	PERCENTAGE OF TOTAL
Abdominal pain, tenderness, rigidity or dullness	82	96
Shock	65	76
Vomiting	23	27
Superficial abrasions	17	20
Left shoulder pain	15	18
Fracture of bones	11	13
Lacerations of other viscera	4	5

Postoperative Results.—The removal of the spleen has apparently not caused any effect on growth or development in the children who have been observed during the postoperative period, in one instance for as long as seventeen years.[4] Minor disturbances which have been noted[4-9] include a secondary anemia, a leucocytosis with a relative lymphocytosis, an occasional eosinophilia, a high reticulocyte count, an increased fragility of the erythrocytes, and a gradual and constant elevation of the platelet count. There has also been noted a hyperplasia of the superficial lymph nodes and of accessory splenic tissue.

SUMMARY

In the analysis of ten cases of traumatic rupture of the spleen among the children in our hospitals and in the review of eighty re-

ports of the same condition in the medical literature, the common diagnostic features have been local abdominal symptoms, shock, vomiting, and left shoulder pain. The frequency with which this last symptom has occurred in these children has demonstrated its diagnostic importance in the consideration of splenic damage whenever an accident involving the left side of the trunk has occurred. Various types of accidents, many of them casual in nature and not productive of much external evidence of severe trauma, caused rupture of the spleen. When the damage of the other organs had not been too great, removal of the ruptured spleen seemed to offer a favorable prognosis and did not cause any demonstrable effect in afterlife.

REFERENCES

1. Homans, John: Textbook of Surgery, Springfield, Ill., 1932, C. C. Thomas Co., pp. 899-900.
2. Robitshek, E. C.: Minnesota Med. **6**: 365, 1923.
3. McCracken, J. C.: Ann. Surg. **79**: 80, 1924.
4. Connors, J. F.: Ann. Surg. **88**: 388, 1928.
5. Kahn, M. H.: Am. J. M. Sc. **165**: 214, 1923.
6. Krumbhaar, E. B.: Am. J. M. Sc. **184**: 215, 1932.
7. Musser, John H.: Arch. Int. Med. **9**: 592, 1912.
8. Pfeiffer, D. B., and Smyth, C. M.: Ann. Surg. **80**: 562, 1924.
9. Shore, B. R., and Kreidel, K. V.: Ann. Surg. **99**: 307, 1934.
10. Baccarini, L.: Arch. Ital. di chir., Bologna **6**: 166, 1922; abst. J. A. M. A. **80**: 360, 1923.

Barnes, Allan F.: Ann. Surg. **59**: 597, 1914.
Bonfield, J. P.: Canad. M. A. J. **32**: 422, 1935.
Butler, Edmund, and Carlson, Everett: S. Clin. North America **6**: 517, 1926.
Connors, J. F.: Ann. Surg. **74**: 1, 1921.
Dretzka, L. J.: Surg. Gynec. Obst. **51**: 258, 1930.
Hamilton, Thomas: M. J. Australia **1**: 439, 1934.
Jackson, T. S.: Surg. Gynec. Obst. **41**: 331, 1925.
Jones, J. F. X.: Am. J. Surg. **38**: 11, 1924.
Kakels, M. S.: New York M. J. **118**: 372, 1923.
Koster, Harry: M. J. and Record **123**: 455, 1926.
Kraft, Rollan Walter: California & West. Med. **34**: 412, 1931.
Lempriere, L. R.: Brit. M. J. **1**: 681, 1923.
Livingston, J.: Brit. M. J. **2**: 16, 1930.
Rosin, I. R.: Brit. M. J. **2**: 1049, 1926.
Smyth, C. M., Jr.: S. Clin. North America **9**: 1181, 1929.
Sorrel, E., Oberthur, M., and Mérigot: Bull. Soc. de pédiat. de Paris **29**: 525, 1931.
Straus, D. C., and Tumpeer, I. H.: S. Clin. North America **9**: 345, 1929.
Stretton, J. L.: Brit. M. J. **2**: 211, 1917.
Weston, Angus: Brit. M. J. **2**: 1142, 1932.

ERYTHEMA INFECTIOSUM

Clinical Observations During an Epidemic

John Mott Rector, M.D.
San Francisco, Calif.

THE erythemas of childhood still give us many a theoretical and practical problem to solve. Atypical epidemics of German measles and to a lesser extent of scarlet fever gave rise not so many years ago to the misnomer of "fourth disease"; erythema infectiosum has been described as the "fifth disease"; and occasionally exanthem subitum is referred to as the "sixth disease."

Infectious erythema is to be differentiated from the other exanthemas and is undoubtedly a separate entity. An epidemic of the disease occurring in San Francisco during the spring and early summer of 1938 occasions the present report. The study constitutes forty-three cases, derived from private and clinic practice, day nurseries, and orphanages. Additional cases observed in the public schools are not included because of incomplete data and lack of adequate follow-up.

HISTORY

Like all conditions that remain unclassified for any length of time this malady has been known by a multiplicity of names which include *Ringelrötheln*, megalerythema epidemicum, *Grossflecken*, exanthema variable, *oerliche Rötheln*, erythema simplex marginatum, *epidemiche Kinderrotlauf*, erythema infantum febrile, and erythema annulare in epidemic form.

The first clear description of erythema infectiosum as well as the name, date from Sticker,[1] a German investigator in 1899. It is true in the preceding decade a few small epidemics of an eruptive disorder which was evidently erythema infectiosum had been reported. These writers described it as "local rubella," that is, peculiarly localized German measles, but reached no definite conclusions concerning it as an entity.[2] Escherich[3] claims that he declared the disease to be "different from rubella," but it was not until Sticker's and later Berberich's studies[4] that the question was definitely settled.

Since the early German and Austrian publications scattered accounts of the disease have appeared in Switzerland, the Netherlands, Italy, and France.[5] The first outbreak in this country took place in Hamburg, N. Y., in the spring of 1919.[6] Subsequent epidemics have been noted in St. Louis, Cleveland, Ogden, Utah, and Branford, Conn.[7] The appearance in such widely separated regions suggests the probability that other epidemics have occurred in the United States but have not been described or classified.

Read before Region IV of the American Academy of Pediatrics at the seventh annual session, Oakland, Calif., April 6, 1939.

EPIDEMIOLOGY

All the available communications on erythema infectiosum report group infections, although the small size, short duration, and relative infrequency of these epidemics point either toward a limited degree of contagiousness or to a lack of general susceptibility to the disease. This is further substantiated by the fact that secondary cases in the same family are uncommon and that only a minor portion of the school population is affected, even though many children attend school while afflicted.

The epidemics usually attain a peak by the third or fourth week and then subside with equal rapidity, the total duration being only a few months or less. The San Francisco outbreak differed in no particular essentials from the others. While only 128 cases were brought to the attention of the Department of Health the actual morbidity was much greater, as it is not a reportable condition. Further, many of the initial cases were not recognized, while others were so mild that they were overlooked. Sporadic cases are still occurring in San Francisco.

In the past some authorities[6] have felt that there was significance in the observation that infectious erythema frequently occurs in conjunction with epidemics of measles, German measles, and scarlet fever. This association has not been apparent in recent epidemics and seems unimportant. An attack of any of the other infectious diseases affords no immunity to erythema infectiosum. The burden of evidence indicates that one attack confers a permanent immunity.[7b] No second attacks have been reported. The duration of infectivity is not known.

ETIOLOGY

Transmission apparently results from a droplet infection, but the specific agent remains unknown. There is a seasonal incidence, the malady being most frequent in the spring. The age group most commonly affected is from 4 to 12 years. It is rare in infants and in adults. Under 6 months of age there appears to be an immunity (Case 1). There is an interesting and decided sex predilection, females being more often afflicted in a ratio sometimes as high as 2 to 1. In one San Francisco school all of the cases observed were in girls. The incubation period has been reported to be from five to fourteen days.[5a, 6] However, in this last outbreak two secondary cases were seen which did not develop until the sixteenth day after exposure. Among the forty-three cases in this study the average period of incubation was from seven to eleven days.

SYMPTOMS

Occasionally there is a mild prodrome with slight malaise and sore throat, but in the vast majority of cases the rash is the first and only symptom noted. It usually makes an initial appearance on the cheeks where it is seen as rose-red maculopapules that rapidly coalesce into a confluent mass with a symmetrical, butterfly configuration. The naso-

labial region is not involved, producing a striking circumoral pallor. In well-marked cases the color changes from rose to a deep cyanotic hue, and the skin is turgid and hot to the touch. The picture is not unlike that of facial erysipelas, but the skin is not sensitive, and there is no burning or itching. In milder cases the patient merely appears flushed or overheated and more closely resembles the facies of scarlet fever. There is no enanthem.

Within twenty-four to thirty-six hours the eruption develops on the trunk and extremities and spreads toward the periphery, the hands and feet being the last portions of the body to be affected. On the trunk the rash is rarely heavy and may be absent. In well-defined cases it appears there as a fine, discreet, maculopapular eruption that is practically indistinguishable from the rash of German measles. The exanthem is quite uniform on the extremities and presents a typical and characteristic picture. It is usually but not necessarily more marked on the extensor surfaces, where it occurs as rather large macules or maculopapules that eventually assume a violaceous tinge. These fade from the center and leave well-defined peripheries which create a peculiar lattice-work pattern (Fig. 1). This maplike or geographic tendency eventually appears in every case of erythema infectiosum. The buttocks frequently show a similar distribution. Whereas the eruption disappears rapidly from the face and trunk, it may last from 6 to 14 days on the extremities, and an interesting evanescence is often seen, the rash fading for hours or days and then reappearing, usually after slight dermal irritation.

Subjective symptoms are practically nil. In those very occasional cases with mild catarrhal manifestations, anorexia may be present. Pruritus is rare. A normal or near normal temperature is the rule, and only 6 per cent have a fever over 100° F.[74] There is no adenopathy or splenomegaly, and the eruption is not followed by desquamation or pigmentation. A moderate leucopenia with a relative lymphocytosis and an eosinophilia is usually found.[6] The eosinophiles vary from 1 to 16 per cent and average from 4 to 6 per cent.

SELECTED CASE HISTORIES

CASE 1.—J. O. was a healthy girl of 9 years with a previous history of measles and German measles. On April 10, 1938, after a brief prodromal period of anorexia and slight malaise, she developed a rash on her face that was characterized by a brilliant flush with a well-defined circumoral pallor. The face looked swollen and was hot to the touch. A faint macular eruption could be detected in the postauricular area. Except for light pharyngeal injection the remainder of the examination was negative. The temperature was 98.8° F. By the following day there was a generalized eruption. On the thorax and abdomen it appeared as a fine, dull red maculopapular exanthem closely resembling the rash of German measles. Over the extremities it was more extensive, especially on the extensor surfaces. On the hands and feet it had a bluish red cast and appeared blotchy. The temperature was again 98.8° F.

The white count was 7,700 with 34 per cent neutrophiles, 42 per cent lymphocytes, 8 per cent monocytes, and 16 per cent eosinophiles. A nose and throat culture showed no unusual organisms. The sedimentation rate (Cutler) was 7 mm. in 60 minutes.

On April 12, forty-eight hours after onset, the rash was beginning to fade from the face and trunk but was still very heavy on the extremities where it had assumed a lacelike or geographic pattern that remained for twelve days (Fig. 1). During this time anorexia and low-grade fever continued. A 3-month-old nursling sister who had been intimately exposed did not contract the disease.

CASE 2.—J. A., a boy of 4½ years of age, suddenly developed a rash on his arms and legs on May 30, 1938. No preceding eruption on the face or trunk had been noticed. A past history of exanthem subitum was elicited. There was no apparent allergic background. The child felt very well, and his temperature was normal. The physical examination was negative throughout except for a mottled, bluish red, maculopapular rash on the extremities and buttocks that showed a characteristic honeycomb patterning. It was most marked on the extensor surfaces of the legs. Pruritus was absent.

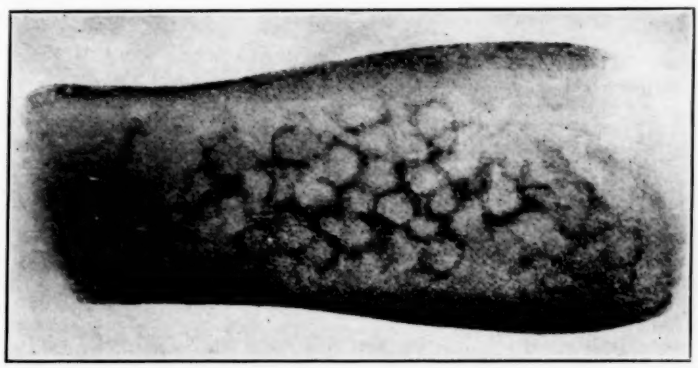


Fig. 1.—Characteristic gyrate pattern, producing typical lacelike appearance.

Leucocytes numbered 7,350 with 47 per cent neutrophiles, 40 per cent lymphocytes, 6 per cent monocytes, and 7 per cent eosinophiles. A nose and throat culture was negative. Erythrocytic sedimentation was 6 mm. in 60 minutes.

Two days later the rash rapidly disappeared only to return in full bloom on the following day. This evanescence continued throughout the remainder of illness, the application of heat or the use of friction bringing the rash out promptly when the skin seemed practically clear. The total duration was eight days.

CASE 3.—H. V. was a 4-year-old girl who had been perfectly well until June 11, 1938, when an eruption appeared on her chest and abdomen and spread rapidly to the extremities. Upon examination the face was a brilliant red and was suffused and swollen with a pronounced circumoral pallor. Over the chest and abdomen there was a fine maculopapular eruption, brownish red in color and quite faint. The rash was much heavier on the extremities, where it was most marked on the flexor surfaces and included the palms and soles. A gyrate effect was already evident.

The white count disclosed 8,900 cells, of which 48 per cent were neutrophiles, 38 per cent lymphocytes, 9 per cent monocytes, and 4 per cent eosinophiles. A nose and throat culture was negative. The sedimentation rate was 7 mm. in 60 minutes.

The eruption was entirely gone from the face and trunk by the third day. On the seventh day it was still present on the extremities but had shifted to the extensor surfaces, where it continued intermittently for another week. During her fourteen days of rash the child was afebrile and had no complaints.

EXPERIMENTAL OBSERVATIONS

Nose and throat cultures, obtained from eleven patients, showed no unusual organisms. These were taken at various stages of the disease and planted on blood agar plates. Sedimentation tests were carried out simultaneously and were all within normal limits, the average being 7 millimeters in 60 minutes (Cutler method).

Using 20 cubic centimeters of sterile physiologic salt solution, nasopharyngeal washings were obtained from an active case on the second day of the eruption. Several cubic centimeters of the washings were then instilled into the nasopharynx of J. O. (Case 1), who had recovered from erythema infectiosum twelve weeks previously. Nothing of note occurred.

DIAGNOSIS

The diagnosis is often not established because the disease picture is not very well known. Salient diagnostic features include the distribution of the rash, its peculiar gyrate pattern, evanescent character, relatively long duration, and asymptomatic course. If the malady, as usual, occurs in small epidemics, the diagnosis is easy.

It is to be stressed that the eruption may vary and show several changes, yet the localization, general appearance and course are typical and fairly constant. Practically the only variations seen are in the extent of the rash (Table I). It is always heavier on the extremities than the body, and frequently more intense on the forearms than elsewhere. If the lower extremities are involved, there is usually a similar rash on the buttocks. The presence of a circinate or latticelike patterning, limited to the extremities or buttocks is essential to diagnosis and eventually occurs in all cases. If the phenomenon of evanescence is present, it is not seen until after gyration has developed.

TABLE I

VARIATIONS IN RASH (43 CASES)

DISTRIBUTION AND CHARACTER	NUMBER OF CASES
Confluent on face, maculopapular on trunk, heavy and gyrate on extremities	26
Finely macular on face, maculopapular on trunk, heavily gyrate on extremities	2
Absent on face, maculopapular on trunk, gyrate on extremities and buttocks	3
Absent on face and trunk, gyrate on lower extremities and buttocks	4
Present only on forearms	8

Erythema infectiosum is to be differentiated from the other acute exanthemas, from erythema exudatum multiforme, and from the various

urticarial dermatoses arising from foods, drugs, and external irritants. In those occasional cases where the eruption fails to become confluent on the face (Table I) German measles may readily be suspected until the characteristic features of the disease become evident. In sporadic cases, if rash is present only on the extremities, confusion with erythema multiforme or urticaria may occur. Here a negative history, asymptomatic course, absence of pruritus, relatively long duration of the eruptive stage, and a normal sedimentation rate will all assist in determining the true nature of the condition.

TREATMENT

Other than mild symptomatic measures no therapy is required. As the condition is infectious, isolation technique should be observed until the eruption has permanently disappeared. Susceptible contacts should be restricted for two weeks.

SUMMARY

Infectious erythema is an acute, moderately communicable disease occurring chiefly in children. The constitutional symptoms are slight and the eruption is the dominant feature.

Based upon a clinical investigation of 43 cases, the characteristics and general course of the malady are described and selected case histories are presented. The results of certain experimental data are included together with epidemiologic and diagnostic considerations.

From a public health standpoint it would seem advisable to create a place for erythema infectiosum on the official list of reportable diseases.

REFERENCES

1. Sticker, G.: Ztschr. f. prakt Aerzt. **40**: 121, 1899 (cited by Rietschel, H.: Med. Klin. **26**: 504, 1930).
2. Tschamer, A.: Jahrb. f. Kinderh. **29**: 372, 1899.
   Gumplewicz, I.: Jahrb. f. Kinderh. **32**: 266, 1891.
   Tobeitz, A.: Arch. f. Kinderh. **25**: 17, 1898.
3. Escherich, T.: Tr. Eleventh Internat. Med. Cong. Moscow, 1896 (cited by Rietschel).
   Escherich, T.: Monatschr. f. Kinderh. **3**: 285, 1904; Wien. klin. Wchnschr. **17**: 631, 1904.
4. Berberich, E.: Eine Epidemie von akutem Erythem bei Kindern (Erythema infectiosum acutum), Diss. Giessen, 1900, cited by Rietschel.
5. (a) Hanneman, Y.: Nederl. tijdschr. v. geneesk. **70**: 1984, 1926 (Abstr., J. A. M. A. **88**: 138, 1927).
   (b) Taccene, G.: Riv. di. clin. pediat. **25**: 145, 1927 (Abstr., J. A. M. A. **88**: 2005, 1927).
   (c) Cathala, J., and Cambessédès, H.: Bull. et mém. Soc. méd. d. hôp. de Paris **52**: 205, 1928.
6. Shaw, H. L. K.: Erythema Infectiosum, Nelson's Loose-Leaf Living Medicine, New York, Thomas Nelson and Sons, Vol. I, p. 911, 1920, Erythema Infectiosum, Abt's Pediatrics, Philadelphia, W. B. Saunders Company, 1924, vol. 5, p. 660.
7. (a) Zahorsky, J.: Am. J. Dis. Child. **28**: 261, 1924.
   (b) Herrick, T. P.: Am. J. Dis. Child. **31**: 486, 1926.
   (c) Smith, E. H.: Arch. Pediat. **46**: 456, 1929.
   (d) Lawton, A. L., and Smith, R. E.: Arch. Int. Med. **47**: 28, 1931.

AMYOTONIA CONGENITA (OPPENHEIM'S DISEASE) OCCURRING IN TWO OF TRIPLETS

AARON GOURSE, M.D.
SACRAMENTO, CALIF.

ALTHOUGH cases of amyotonia congenita occurring in identical twins have been reported by Forbus and Wolf[1] and in a twin boy and girl as reported by Pearce,[2] a perusal of the literature fails to reveal any report of the condition occurring in only one of the twins or in triplets. This report is of interest because of the occurrence of amyotonia congenita in identical twins born with a triplet but absent in the third child. The identical twins are girls and the triplet is a boy.

CASE REPORT (THE "T" FAMILY)

Family History.—Both parents are living and well. The father was 29 years old and the mother was 26 years old at the time of conception of the triplets. The mother has had no miscarriages, and her blood Wassermann was negative two months before the triplets were born. There is one more child, a male, who is 4½ years older than the triplets. His growth and development have been normal. As far as could be determined, no relatives of the family had ever had any signs or symptoms suggestive of amyotonia congenita.

Birth History.—The mother's prenatal condition was entirely normal until three weeks prior to labor when a slight pitting edema of the ankles appeared. Blood pressure and urine were normal. When she was admitted in labor to the ward, her blood pressure was 130 systolic and 80 diastolic, the highest that had been recorded. She was in labor only two hours and thirty-five minutes. The first infant, a female was born in the right occipitoanterior (ROA) position. This was immediately followed by the second female with a similar position. The male was in the left sacroanterior (LSA) position and was delivered by breech extraction. One Schultze placenta was then delivered which contained one chorion, two amniotic cavities and two cords which had been attached to the girls. A second Schultze placenta with a single cord followed. The triplets were born May 28, 1935; two girls were named Ruth and Ruby, respectively, and the boy was named Richard. At birth Ruth weighed 3 pounds and 12 ounces, Ruby 3 pounds and 10 ounces, and Richard 5 pounds and 6 ounces.

Personal History.—The triplets first came under my observation Oct. 7, 1936, when they were 16 months old. At that time the girls were much smaller and less well developed than the boy. The girls had been fed only their formula and an occasional teaspoonful of cod liver oil. Other foods when given were vomited —including the orange juice. The girls had had only artificial feeding while Richard had nursed at the breast until he was 3 months old.

Physical Examination.—At the time I first saw them, Richard was well developed and well nourished and apparently normal. He weighed 25 pounds. Ruth weighed 13 pounds and 8 ounces, and Ruby weighed 14 pounds and 8 ounces.

The following findings were identical for both girls, except where otherwise stated. They were poorly nourished and underweight. The head was narrow and long, the anterior fontanel admitted the tip of a finger, and the posterior fontanel was closed. The upper central and lateral incisor teeth and the lower

From the Department of Pediatrics, Sacramento County Hospital.

central incisors were present. The epiphyses of the wrists were enlarged and the proximal phalanges of the second, third, and fourth fingers of both hands were enlarged, and the fingers tapered to the tips. These fingers could not be fully extended and always remained slightly flexed when the hands were opened. There was a symmetrical weakness of both legs, but not complete paralysis. When the girls were lying on their backs, their legs were held vertically in the air and there was extreme flaccidity which allowed the hips to be flexed so that the ears could be rubbed with the soles of the feet without difficulty. No atrophy of the muscles was apparent. The girls were unable to sit up voluntarily although Ruth could remain in the sitting position if so placed much better than Ruby, while Richard was able to sit up and stand and tried to walk. Knee jerk, ankle jerk, and the triceps reflexes were all normal. The abdominal reflexes were not demonstrated because of crying. There was no loss of sensation to pain and touch. X-ray films of the hips and skulls of both girls and of Ruth's hands were negative, but the wrists showed some rachitic changes.

Fig. 1.—Triplets at the age of 2 years.

Subsequent Course.—There was gradual improvement in the condition of the girls and they became stronger. The development of the power of locomotion of the girls from early infancy is of interest. At the age of 20 months it consisted of rolling over and over until they arrived at their destination. Later they pulled themselves, snakelike, flat on the abdomen. This was followed by crawling on the hands and knees. When the girls were 29 months old, movement was on the hands and feet, and they were still unable to stand erect unless holding to something. When 34 months old they were able to stand and walk a few steps without holding to anything, but were unable to stand erect. They stood in a semi-

crouched position. At 36 months they could stand and walk alone, and when 40 months old they could run. Richard sat up without assistance at 6 months and could stand at 10 months and walk at 18 months.

When the girls were 3 years old, their legs could no longer be placed in the peculiar positions previously described.

Although the superficial reflexes have always been normal, the deep reflexes have varied at different examinations, at times being active and at other times absent.

All deciduous teeth were present at 34 months and were in good condition, but crowded. Richard had all of his teeth at 23 months.

Fig. 2.—Ruby and Ruth at 29 months.

Fig. 3.—Ruby and Ruth at 29 months.

All three of the triplets had whooping cough at 34 months, and then Ruth showed evidence of becoming pigeon-breasted, the sternum being pushed forward and the costal margins flaring out. There was no beading of the ribs. Her abdomen was very large—a pot-belly. Ruby did not develop the pigeon-breast, and Ruth improved very much so that at present both girls have little deformity of the chest other than a moderate flaring out of costal margins.

The triplets had measles when 45 months old and made an uneventful recovery.

The girls were unable to speak until they were 3 years old and now when nearly 4 years old their talking is limited to only a few words. Richard speaks very well for his age.

Laboratory Examination.—Routine blood counts, urinalysis, and spinal fluid examinations were normal. Spinal fluid Wassermann and Kahn tests were negative. Blood typing (Moss classification) on April 26, 1937, showed that all the triplets and the mother were Type 2 and the father was Type 4. These examinations were made by Miss Ruth Sedell, technician at the Sacramento County Hospital.

Blood chemistry by Dr. Paul W. Christman in December, 1937, showed normal sugar, nonprotein nitrogen, chlorides, serum phosphates, and serum calcium for the triplets, and the calcium-phosphorus product was normal for each of them.

Magnesium content of the blood was determined by Dr. David M. Greenberg of the University of California at Berkeley in December, 1937. The whole blood magnesium, the plasma magnesium, and red corpuscle magnesium were almost identical in each case for the triplets and were normal.

X-ray films of the wrists June 8, 1938, were reported by Dr. John D. Lawson as showing normal growth and development with no signs of rickets.

Blood chemistry by Dr. Paul W. Christman showed the following results:

Dec. 14, 1937	*Ruth*	*Ruby*	*Richard*
Sugar (mg. %)	81	84	94
Nonprotein nitrogen (mg. %)	29	29	24
Chlorides (mg. NaCl per 100 c.c. of whole blood)	487	446	436
Dec. 23, 1937			
Serum phosphates (mg. %)	4.60	4.80	5.11
Serum calcium (mg. %)	10.10	10.05	10.25
Calcium-phosphorus product	46.4	48.1	52.3

Blood chemistry by Dr. David M. Greenberg of Berkeley, California, showed the following results:

Dec. 14, 1937	*Ruth*	*Ruby*	*Richard*
Whole blood magnesium (mg. %)	4.65	4.64	4.64
Plasma magnesium (mg. %)	Specimen hemolyzed	2.90	3.00
Red corpuscle magnesium (mg. %)	Specimen hemolyzed	8.4	8.1

DISCUSSION

Numerous theories concerning the etiology of amyotonia congenita have been developed. Oppenheim[3] believed that the disease was due to arrested development of the muscle tissue. Baudoin[4] thought that the cord was primarily involved. Marburg[5] considered the disease to be a form of chronic infantile anterior poliomyelitis. Gurdjian[6] advanced the theory that a toxic factor involving the neuromuscular system and associated with a familial tendency to the disease may be responsible for amyotonia congenita. According to Reuben,[7] primary abiotrophy of the musculature and secondary failure of proper development of the whole nervous system was the pathogenesis. Faber[8] believed that the original fault lay in a defective germ plasm of reproductively exhausted parents, with the primary lesion congenital hypoplasia of the lower motor neuron, the changes in the muscles being secondary. Forbus and Wolf[1] express the opinion that amyotonia

congenita is the result of some injury to the developing embryo which localizes especially in the anterior horn of the gray matter of the spinal cord, the condition of the muscles being secondary to this injury.

My cases show that amyotonia congenita can occur in identical twins but be absent from a third child born of the same pregnancy but from a different ovum. An injurious agent likely to injure and produce identical defects in two embryos in the same uterus would be likely to injure the third embryo in the uterus particularly if the injurious agent were transmitted through the placenta from the mother. If some element was left out or some derangement occurred in the embryo, it must have occurred very early in the life of the embryo, in fact within that period when the individual cells formed by the developing ovum still possess their totipotency and are capable of giving rise to complete individuals. Only by accident or chance could the disease have occurred in this manner and produced identical findings in the twin girls.[1] Inasmuch as one child is normal, it would be more likely that the abnormality was present in the fertilized ovum or zygote or that there was a defect in the germ plasm of one or both parents prior to conception.

Hurwitz and Gerstle[9] called attention to the possible significance of amyotonia occurring most frequently in persons whose blood is of Type 2. In my cases, as in theirs, the affected children and one of the parents were Type 2. Hurwitz and Gerstle reported a decrease in the magnesium content of the red blood cells. Such findings were not confirmed by my cases in which the magnesium results were the same for the girls with amyotonia congenita and the normal triplet.

SUMMARY

Amyotonia congenita (Oppenheim's disease) is reported as occurring in identical twins born with a triplet but absent in the third child.

These findings appear to substantiate Faber's theory that amyotonia congenita is due to a defect in the germ plasm of the parents.

A similarity of blood grouping, Type 2 (Moss), between one parent (the mother) and the affected children was present.

Blood magnesium determinations were the same for the twins with amyotonia congenita and the normal triplet.

REFERENCES

1. Forbus, W. D., and Wolf, F. S.: Bulletin of the Johns Hopkins Hosp. **47:** 309, 1930.
2. Pearce, N. O.: Am. J. Dis. Child. **20:** 393, 1920.
3. Oppenheim, H.: Monatschr. f. Psychiat. u. Neurol. **8:** 232, 1900.
4. Baudoin, A.: Semaine méd. **37:** 241, 1907.
5. Marburg, O.: Arb. a. d. Neurol. Inst. a. d. Wien. Univ. **19:** 133, 1911.
6. Gurdjian, E. S.: Arch. Neurol. & Psychiat. **24:** 52, 1930.
7. Reuben, M. S.: Arch. Int. Med. **20:** 657, 1917.
8. Faber, H. K.: Am. J. Dis. Child. **13:** 305, 1917.
9. Hurwitz, Samuel, and Gerstle, Mark, Jr.: Arch. Neurol. & Psychiat. **333:** 1317, 1935.

AMYOPLASIA CONGENITA (ARTHROGRYPOSIS MULTIPLEX CONGENITA)

HARRY S. ALTMAN, M.D., AND LEONARD T. DAVIDSON, M.D.
NEW YORK, N. Y.

THE term amyoplasia congenita designates a symptom complex which includes congenital, symmetrical joint rigidities of various degrees, always without inflammatory changes. A congenital myodystrophy of this kind was first described by Otto in 1841, and in 1905, Rosenkranz collected fifty-six cases which were similar in nature and which he called "arthrogryposis multiplex congenita." From then until 1936, similar conditions were described by various authors, but under different names, such as amyoplasia congenita, multiple congenital articular rigidity, and myodystrophia foetalis deformans.

REPORT OF A CASE

This patient, when first seen by one of us, was 2 weeks of age. The birth history was entirely normal; his birth weight was 3000 gm. At the time of the examination, the mother had noticed nothing unusual and had brought him in for a routine checkup. The weight at this time was 3180 gm. The height was 51.5 cm. He was rather spastic and did not seem to be able to raise his upper eyelids. The feeding history seemed quite normal. At subsequent monthly examinations, his spasticity became more noticeable, and at the age of 5 months he showed a definite inability to extend his legs, to flex his fingers, and there was a marked ptosis of both lids. He vomited frequently during these months. He was very spastic, and the skin seemed to be thickened, resembling that of scleroderma. At the age of 10 months, he was referred to the Pediatric Division of Vanderbilt Clinic, and on examination there, he was found to weigh 6840 gm., and was 62 cm. tall. The biceps and triceps reflexes were present, but the knee jerks could not be obtained. The fingers were more rigid and could be flexed only by force. The legs were held in flexion of about 75 degrees, and they could not be extended, even by force. The expression was that of a child who was mentally subnormal, but this fact was not corroborated by an intelligence test done at a little later date. No definite diagnosis was made at this time, but baking and massage were instituted for a period of three months, and then he was admitted to the Babies' Hospital for further study. The examination at this time revealed that all four extremities were spastic. His lower extremities showed bilateral clubfeet and contractures of the hamstring muscles. The upper extremities likewise showed contractures and absence of cortical movements of both hands. The reflex threshold was tremendously increased. The abdominal reflexes were diminished. Sensation seemed normal. A bilateral ptosis was present (Fig. 1). The distal portions of all four extremities were cold. The skin over the trunk had the quality of scleroderma; it was tight and could not be picked up in folds. A pneumoencephalogram, done at this time, showed the presence of more air in the right hemicranium than in the left, but the depth of the subarachnoid space did not warrant a diagnosis of brain atrophy. The spinal fluid findings were

From the Babies' Hospital and the Department of Pediatrics, Columbia University.

entirely normal. The neurologist's opinion was that the patient had a cerebral agenesis with a third nerve lesion, probably nuclear in origin. An ophthalmologist corroborated the diagnosis of congenital bilateral ptosis. He found no gross limitation of mobility in any direction of gaze. He believed that the patient had a definite pallor of the optic discs, more pronounced on the left, probably due to partial atrophy. It was thought that the ptosis occurred as a nuclear affection of congenital origin. No explanation could be found for the partial atrophy of the optic nerve.

From the age of 10 months to 3 years, he received massage and postural correction fairly consistently, and he gradually became able to put his heels to the ground when walking, though the knees were held slightly flexed. He was still quite spastic. He was able to hold objects in his hands, even a ball. There was no change in the ptosis (Fig. 2). A psychometric test done at 3 years of age gave him a rating of 120. The boy did well from then until he reached 7 years of age, when he was again asked to come in for a check up. At this time, the patient was described as a slender, 7-year-old boy who appeared fairly well developed, but had striking abnormalities of his muscular system. The skin seemed rather tight, but not definitely abnormal.

Fig. 1.

Fig. 2.

Fig. 1.—Patient at 11 months of age, showing flexed knees, rigid fingers, and flexed elbows.

Fig. 2.—Showing ptosis and rigid fingers, with absence of folds of skin over interphalangeal joints. Age, 3 years.

There was a bilateral ptosis of both eyelids, and he could not look straight forward unless he tilted his head backward or elevated his lids with his frontalis muscles. The pupils were equal and reacted promptly and equally to light and accommodation. The extraocular movements were normal. The fundi did not show evidence of optic atrophy as previously reported. He had the normal number of teeth for his age, and they were in good condition. His tonsils were enlarged, rather ragged, and injected. The heart and lungs were normal. The abdomen was normal, and the

liver, spleen and kidneys could not be felt. The genitals were normal. The spine was straight, but there was some limitation of anterior flexion. The neck movements were normal. The range of motion of the scapulae seemed limited. The shoulder movements were normal. There was a slight limitation of about 5 or 10 degrees in

Fig. 3.—Note the curving in of both little toes and the tense skin over the phalanges

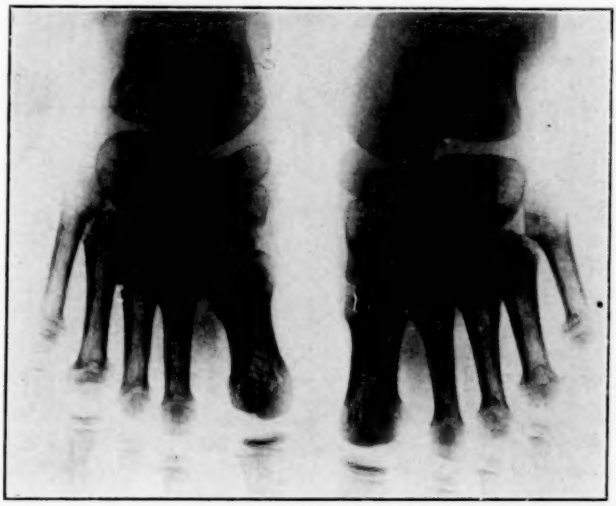


Fig. 4.—Note the cuneiform bones with their punched-out defects.

both flexion and extension of the elbows. He could not touch his fingers to his shoulders. There was normal pronation of the forearms but slight limitation of supination. The movements of the wrists were normal, except for some limitation of extension. Abduction and adduction of the fingers were normal. He could flex his fingers at the metacarpophalangeal joints, but active motions of the interphalangeal joints were practically absent. His fingers were stiff, and, although they could be

flexed to some extent, they could not be brought into the palm. The motions of the hips were normal, and there was no adductor spasm. There was about a 10 degree limitation of extension in both knees. Very little active or passive motion could be elicited in either foot or ankle. The right foot could not be dorsiflexed to a right angle. Flexion of the left foot was 10 degrees less than that of the right. The arches of both feet were high. The movements of the toes were considerably limited. Both little toes curved in (Fig. 3). All the muscles were firm and felt somewhat rubbery. There was generalized muscular atrophy. The neurologic examination showed that the biceps, triceps, and knee jerks were equal, but rather inactive. The abdominals were equal and active. There was no nystagmus. There were no cerebellar signs. The Romberg sign was negative. His gait was somewhat awkward because of the limitation of motion in the ankles.

Fig. 5.—Note flexion at knees and inability to lower heels to ground.

The roentgenographic examination showed that the maturation of the skeleton was normal. All of the long bones of the hands had a tendency to rectangular contours, with obliteration of the normally concave lateral borders. This is best seen in the fifth metacarpal on each side. The distal ends of both ulnae showed roughened margins with slight lateral bowing. On the ulnar side of the distal ends of both radii, there were well developed short spurs which projected obliquely, laterally, and cephalad. Both feet appeared normal, with the following exceptions: There was definite spreading of the distal ends of the metatarsals; this lesion was best developed in the distal end of the fourth left metatarsal and in the distal ends of the fourth and fifth right metatarsals. The medial cuneiform bones of both feet (Fig. 4) were pathologic; on the left side, there was a punched-out effect medially, with a surrounding zone of sclerotic bone and fragmentation. The right medial cuneiform

showed a marked irregularity in density, and at the junction of the caudal third with the rest of the bone, there was fragmentation. The lateral cuneiform on the left showed a cystic area of negative density approximately 1 cm. in diameter.

The blood count and the urinalysis were normal. The tuberculin and Kahn tests were negative. The serum calcium level was 10.9 mg. per 100 c.c. and the serum phosphorus level was 5.1 mg. per 100 c.c. A biopsy of the triceps and gastrocnemius muscles showed the muscle fibers to be of normal color and consistency, and on microscopic examination there was no fibrosis or fatty displacement.

An examination at 8 years and 3 months of age showed him to be very markedly improved and able to carry on almost all the activities of any boy of his own age. He was somewhat spastic. His skin was still a little firm, and there were no wrinkles over the intraphalangeal joints of either the hands or feet (Fig. 5). The knees and elbows were held slightly flexed. Ptosis was still present (Fig. 6), and the fundi were entirely normal. A roentgenographic examination of the hands and feet at this time showed no abnormalities of the tarsal, metacarpal or metatarsal bones but revealed some cystic changes in the lateral cuneiform bones. The medial cuneiform bones were now entirely normal. An intelligence test performed again gave him a rating of 120.

He is to have plastic surgery performed very shortly.

Fig. 6.—Patient at 8 years and 3 months of age; ptosis is still marked.

COMMENT

There is considerable difference of opinion as to the underlying causation of this condition. Most observers are in agreement that the muscles are primarily at fault and that the joints are secondarily involved.

In 1905, Rosenkranz, in writing on clubhands and contractures of the upper extremities and lower extremities, tried to explain the cause of the deformities in question. He recognized the clinical fact that weakness, wasting, and sometimes complete paralysis of muscles were present, and he attributed the contractures to a paralysis of neurogenic origin,

analogous to that of infantile paralysis, and to a failure in the development of the central nervous system.

Lewin, in 1925, wrongly conceived that the joints were primarily at fault and coined the unfortunate appellation "arthrogryposis multiplex congenita," the name by which the deformity is usually known at the present time.

Most workers feel that the primary defect in this syndrome is an aplasia, or failure of development of the muscles, presumably originating early in embryonic life. Sheldon was the first to put forward the hypothesis that the muscles were primarily at fault and that the defects in the joints were a secondary result. He confirmed his ideas by investigating the electrical reactions of the affected muscles, which showed no reaction of degeneration and weak or absent faradic responses.

Middleton seems to be the only one who favored the idea that the process is entirely one of muscle degeneration occurring late in intrauterine life, after the muscles are fully differentiated. He recognized the muscular defects, but stressed the association of the clubfeet and clubhands, without any bony aplasia to account for their presence. The clubfoot in this disease differs from the ordinary variety of talipes equinovarus in the absence of muscular power. Middleton at first thought that an early cessation of development of muscle fibers at the myoblastic stage was responsible for the deformities. His later observations on premature lambs with a comparable syndrome suggested that the process was one of degeneration of formed and differentiated muscle fibers and not a myoblastic dysplasia. The sections showed that all muscles, though abnormal, were present.

It would seem, therefore, that the term "amyoplasia," as suggested by Sheldon in 1932, is most descriptive of the condition. The limb muscles are usually alone affected, due to the fact that the muscles of the limb buds are a later development than those of the trunk and arise from a different source.

In 1936 Cook, in her report of a case, summarized her criteria for making the diagnosis of amyoplasia congenita as follows:

1. Congenital joint rigidities of varying degrees, usually symmetrical, and always without inflammatory changes.
2. Hypoplasia or degeneration of those muscles which normally produce the movements which the child is unable to perform.
3. Absence of any hypertonia and hypertrophy of antagonistic muscles, showing that the immobility is not attributable to muscle overaction.
4. Weak or absent faradic responses in affected muscles, with no reaction of degeneration.
5. No sensory or trophic changes.
6. Normal intelligence.
7. Extensive fibrofatty changes in the affected muscles.

While the definite diagnostic criteria of Cook can be applied to amyoplasia congenita cases, yet not all cases meet all of those requirements. Most of the published cases have shown clubfoot and clubhand, but they are not an essential accompaniment to this syndrome. In the case recorded here, the findings are in accordance with the generally accepted criteria, except that there was no clubbing of the hands and no histologic changes in the muscles. The patient, however, had as no other case recorded has shown, bilateral ptosis, along with an inability to raise his eyes above the level of the horizontal visual axis. The early bony defects, as shown by the roentgenograms, could not be explained. These and the eye condition, may be coincidental, and possibly unrelated phenomena.

SUMMARY

A case of amyoplasia congenita, with congenital ptosis of both eyelids, which improved under physiotherapy, is reported.

REFERENCES

1. Rocher, H. L., and Ouary: Arch. franco-belges de Chir. **32:** 256, 1930.
2. Cook, Elsie: Arch. Dis. Child. **2:** 261, 1936.
3. Kheyfits, A. B.: Novy khir. arkhiv. **35:** 261, 1935.
4. Khurgin, M. A.: Sovet. khir. **8:** 100, 1935.
5. Rocher, H. L.: J. de méd. de Bordeaux **88:** 772, 1913.
6. Middleton, D. S.: Edinburgh M. J. **41:** 401, 1934.
7. Price, J.: Arch. Dis. Child. **8:** 343, 1933.
8. Sheldon: Arch. Dis. Child. **7:** 117, 1932.
9. Lewin, P.: J. Bone & Joint Surg. **23:** 630, 1925.
10. Stern, W. A.: J. A. M. A. **81:** 1507, 1923.
11. Rosenkranz: Ztschr. f. orthop. Chir. **14:** 52, 1905.
12. Middleton, D. S.: Edinburgh M. J. **39:** 389, 1932.
13. Huenekens and Bell: Am. J. Dis. Child. **20:** 496, 1920.
14. Scarlini, G.: Arch. di ortop. **42:** 451, 1926.

CHYLOTHORAX

Review of Literature and Report of Case in Newborn Infant

James K. Everhart, M.D., and Alvin H. Jacobs, M.D.
Pittsburgh, Pa.

ONLY one of the sixty-nine instances of effusion of chyle into the pleural cavity recorded in the past 300 years has occurred in a newborn infant. It is felt, therefore, that it is justifiable to report the occurrence of another such case in a newborn infant.

CASE REPORT

J. S., a 15-day-old white male, was admitted to the Children's Hospital of Pittsburgh, service of Dr. J. K. Everhart, March 10, 1939, because of cyanotic spells. The patient was born at home following a 14½-hour uncomplicated labor. At birth, the umbilical cord was wound tightly about the child's neck, causing extreme cyanosis of the head and neck and necessitating vigorous efforts on the part of the accoucheur to revive the child. Because of the spells of cyanosis which occurred each time the baby cried, x-ray pictures of the chest were taken; a diagnosis of congenital atelectasis was made, and the patient was referred to the Children's Hospital for treatment. The baby had been breast fed up to the time of admission to the hospital. The family history revealed that the parents were in good health and had two other healthy children.

Physical examination on admission revealed a 2-week-old infant, weighing 8 pounds and 4 ounces, who did not appear to be acutely ill. He was breathing with ease but became somewhat cyanotic when crying. The rectal temperature was 98.4° F. The positive physical findings were limited to the chest, examination of which revealed diminished excursion of the right side with markedly impaired percussion note and faint, jerky breath sounds in this area. The left lung was apparently normal. The point of maximum impulse of the heart was beyond the nipple line on the left side. These findings indicated a right-sided pleural effusion.

Laboratory data showed the urine to have a one-plus sugar reaction. Blood count showed a hemoglobin of 19 gm.; erythrocytes, 5,450,000; leucocytes, 7,200; polymorphonuclear neutrophiles, 56 per cent; lymphocytes, 34 per cent, and eosinophiles, 4 per cent. Tuberculin test with P.P.D. was negative.

Roentgenologic examination of the chest revealed an unexpanded right lung with a dense shadow along the lateral chest wall on that side. The heart and mediastinum were displaced toward the left side. The picture was that of pleural effusion in the right chest.

On the third day after admission, thoracentesis was done with the removal of 110 c.c. of milky fluid from the pleural cavity. Immediately after the withdrawal of the fluid, the right lung expanded, and the mediastinum returned toward its normal position.

The fluid removed from the chest was milky with a yellowish tint and had no odor. A small amount of fine coagulum formed on standing and settled to the bottom of the tube, together with a few red blood cells. After standing at room

From the Children's Hospital of Pittsburgh and the Department of Pediatrics, School of Medicine, University of Pittsburgh.

temperature for many weeks, there was no change in the character of the fluid, and no putrefaction took place. It had the physical properties of a true emulsion. Smears of the fluid stained with Wright's stain showed a few cells, mostly lymphocytes, with an occasional red blood cell and polymorphonuclear leucocyte. Smears stained with Sudan IV revealed abundant small fat globules. Chemical characteristics of the fluid were as follows: specific gravity 1.014, pH 7.4, fat content 2.5 per cent, albumin 2.97 gm. per 100 c.c., globulin 3.2 gm. per 100 c.c., total protein 6.17 gm. per 100 c.c., cholesterol 200 mg. per 100 c.c., and lecithin 36.5 mg. per 100 c.c. These chemical and physical properties are typical of chyle and thus establish the diagnosis of chylothorax.

Within three of four hours of the thoracentesis, the marked signs of effusion in the right pleural cavity returned; until he died, it was necessary to tap the patient's chest once every twenty-four to thirty-six hours in order to relieve the dyspnea. Each time the chest was tapped, 50 to 100 c.c. of fluid were removed. From the fifth to the tenth day in the hospital, it was necessary to keep the patient in an oxygen tent. Although the baby took optimum caloric diet consisting of an evaporated milk formula, he continued to lose weight, dropping from 8 pounds and 4 ounces to 6 pounds and 12 ounces.

On the seventeenth hospital day, the patient began to have a fever of about 102° to 103° F., and his abdomen became distended. Death occurred on March 31, 1939, twenty-one days after admission and on the child's thirty-sixth day of life.

Autopsy was performed one-half hour after death by Dr. Maud Menten and Dr. D. W. Whitaker. The right thoracic cavity contained a small amount of chylous fluid, and there was a white exudate over the pleural surfaces which appeared to be fatty in nature. The abdomen also contained a small amount of chylous fluid. Application of pressure at the base of the mesentery in the region of the cisterna chyli resulted in leakage of chylous fluid into the right pleural cavity from a point in the posterior mediastinum 1½ inches above the diaphragm. However, on very careful dissection of the mediastinum, the thoracic duct could not be found. Therefore, it was necessary to assume that there was a leak in the duct in the region of the seeping point in the mediastinum. The only other pathologic findings were a few small areas of terminal bronchopneumonia. There was no evidence of any condition which could have caused obstruction of the thoracic duct.

In 1899 Handman reviewed the medical literature of the preceding 261 years and found reports of 41 undoubted cases of chylothorax. From 1900 up to the time of Lewin's review in 1916, 10 additional cases were reported. From 1916 to the present time we have been able to find 18 additional cases in the literature.

A review of the entire medical literature reveals a total of five cases occurring in infants under one year of age. In 1902, Muttermilche reported the condition in a 5-month-old child following a fall out of bed. In 1908 Jennings reported the condition in a 9-month-old infant, and in 1917, Pisek saw chylothorax in an infant of 9 weeks. Pisek's case was spontaneous in origin and ended in complete recovery. Foley, in 1933, reported spontaneous effusion of chyle in a 9-month-old child.

In 1926, Stewart and Linner reported the occurrence of chylothorax in an infant who developed the signs of pleural effusion on the fourth day of life. There was no history of trauma. Treatment con-

sisted of repeated chest taps, but the patient died on the twentieth day of life. In agreement with our experience, Stewart and Linner were unable to locate the thoracic duct at autopsy.

In the 1- to 14-year age group, there have been ten cases of chylothorax. Most of these patients have been more than 5 years of age, and the chylothorax has resulted either from trauma or tubercular lymph nodes.

ETIOLOGY

The causes of all the undoubted cases of chylothorax were as follows:

Trauma	24 cases
Pressure from neoplasm or tuberculous nodes	13
Secondary growths in the duct	9
Thrombosis of left subclavian vein	4
Perforating lymphangitis	2
Aneurysm-like dilatation of duct	2
Thrombosis of the duct	1
Operation for removal of carcinomatous lymph nodes in the neck	1
Obstruction to radicles of duct from inflammatory thickening of mesentery	1
Filaria	1
Bullet wound	1
Severe cough	1
Spontaneous	4
Cause not determined	5
Total number of cases	69

Many of the traumatic cases were the result of a crushing force and were associated with considerable injury to structures other than the thoracic duct, especially fractures of the ribs and spine. There were, however, a number of cases in which the force was not violent and there had been no injury to any other structures. This group suggests the probability of rupture of the duct due to sudden changes of intrathoracic pneumohydrostatic pressure. This mechanism may also account for the occurrence in one instance of chylous effusion following a severe coughing spell. Various types of tumors in the mediastinum as well as tuberculous lymph nodes have caused chylothorax either by pressure on the duct with rupture below the point of compression or by actual erosion of the duct by the tumor. Schultze reported a substernal goiter as a cause of chylothorax.

Four of the cases listed above were thought to be spontaneous as no cause for the effusion could be found. Whether these cases are

due to pressure changes or to some disease condition of the duct itself is not known. In Stewart and Linner's report of chylothorax in a newborn infant one might postulate a congenital defect in the duct, although this could not be proved at autopsy. In our case, one may postulate a rupture of the duct due to the trauma that the patient was subjected to following delivery.

DIAGNOSIS

The diagnosis of chylothorax depends upon the chemical and physical properties of the fluid removed by thoracentesis, the latter procedure being indicated by the presence of the typical physical signs of pleural effusion. A nonpurulent milky fluid removed from the chest may be either true chyle or chyliform fluid. The former arises from the thoracic duct, whereas the latter is merely a serous effusion in which chemical changes within the fluid, especially in the proteins, result in a lecithin-globulin combination which imparts a milky appearance to the fluid. True chyle is an emulsion of fine fat globules in lymph. It has a specific gravity of more than 1.012, while chyliform effusions usually are below 1.012. Chyle is very slightly more alkaline than blood serum, its pH being about 7.4. On standing, true chyle does not undergo putrefaction. There may or may not be a layer of cream on standing. The presence of the cream layer is often given as diagnostic of chyle, but this is not necessarily true, as the cream stratum may consist of protein granules as well as of fat.

Microscopically, one can see the fat globules in true chyle, the globules staining readily with the ordinary fat stains. The cells present are predominately lymphocytes.

Chemical analysis reveals a high fat content with a high cholesterol and a low lecithin content. In contradistinction to this, chyliform effusions have a very low fat content, a low cholesterol and a high lecithin content. The protein fraction of chyliform fluid is chiefly globulin, while chyle contains relatively more albumin. The following table summarizes some of the chemical findings in the cases of chylothorax that we have reviewed:

Specific gravity	1.012 to 1.018
Albumin	0.495 to 3.9 gm. per 100 c.c.
Total protein	3.0 to 8.0 gm. per 100 c.c.
Fat	0.9 per cent to 4.8 per cent

TREATMENT

The treatment of chylothorax has been unsatisfactory as shown by the mortality rate of 50 per cent. The recommended procedure is repeated thoracentesis. Most authors suggest that taps be performed only as frequently as is indicated for the relief of dyspnea. In oc-

casional cases, spontaneous cure has followed one or two taps. Some authors have also utilized low fat diets in an attempt to reduce the flow of chyle, but this end does not seem to have been accomplished. Operative repair or ligation of the duct has never been attempted because of the formidable approach.

In order to maintain the nutrition, it has been advised that the uncontaminated chyle removed from the chest should be re-introduced intravenously. This same result can be accomplished by the intravenous introduction of fats by the method of Holt.

SUMMARY

1. A case of effusion of chyle into the right pleural cavity in a newborn infant is reported.

2. A complete survey of the literature reveals that 69 cases of chylothorax have been reported. Ten of these cases occurred in children between the ages of 1 and 14 years, five in infants under 1 year of age and one in a newborn infant.

3. The etiology of the chylous effusion in the present case is postulated as being due to the severe trauma at and immediately after birth.

REFERENCES

1. Bargebuhr: Deutsche Arch. f. klin. Med. 1895.
2. Beatty: J. Thoracic Surg. **6**: 221, 1936.
3. Drey: Monatschr. f. Unfallh. **27**: 241, 1920.
4. Foley: Prensa méd. argent. **20**: 62, 1933.
5. Heppner: J. A. M. A. **102**: 1294, 1934.
6. Hussy: Jahrb. f. Kinderh. **87**: 491, 1918.
7. Jennings and Rich: Arch. Pediat. **25**: 195, 1908.
8. Lewin: Am. J. M. Sc. **152**: 71, 1916.
9. Lillie and Fox: Ann. Surg. **101**: 1367, 1935.
10. MacNab and Scarlett: Canad. M. A. J. **27**: 29, 1932.
11. Muttermilch: Ztschr. f. klin. Med. **46**: 122, 1902.
12. Paitre: Bull. et mém. Soc. nat. de chir. **55**: 813, 1929.
13. Pisek: Arch. Pediat. **34**: 929, 1917.
14. Schranz: Klin. Wchnschr. **2**: 1699, 1924.
15. Schultze: Wien. klin. Wchnschr. **38**: 455, 1925.
16. Shackelford and Fisher: South. M. J. **31**: 766, 1938.
17. Sherman: Arch. Pediat. **24**: 646, 1907.
18. Stewart and Linner: Am. J. Dis. Child. **31**: 654, 1926.
19. Van Nuys: California & West. Med. **34**: 369, 1931.
20. Watts: Ann. Surg. **74**: 691, 1921.

PNEUMOCOCCUS (TYPE III) MENINGITIS WITH RECOVERY

STEWART H. WELCH, M.D., AND HENRY F. MARTIN, M.D.
BIRMINGHAM, ALA.

J. R. M., aged 9 years and 2 months, was a robust boy who had been under the care of Dr. Welch since he was 8 weeks old.

Past History.—He had had allergic manifestations, infantile eczema, of short duration around the fifteenth month; and on June 16, 1932, when he was a little over 3 years old, a Schick test had been followed in about twenty minutes by dyspnea, dusky cyanosis, and swelling of the face and lips. The test and control gave strong four-plus reactions. Three infections of the middle ear required drainage. Tonsils and adenoids had been removed when he was 3½ years old. Both drums were freely incised at that time on account of ear discharge that had persisted five or six weeks.

On Dec. 24, 1937, he developed measles. Recovery was a little slow but apparently satisfactory.

Present Illness.—On Feb. 5, 1938, the right eardrum was red and required paracentesis three days later. It drained profusely but required reopening two or three times. He was in school most of the time. On February 18 he complained of pain high in right frontal region and in the right cheek, well defined, opposite the first molar. The ear was more freely incised. The discharge was thick and could be wiped out in long mucous strings. The following day a roentgenogram showed the right mastoid cloudy, and hospitalization was advised because of undue pallor and lassitude.

Previous examination and his examination at 3 P.M. in the hospital failed to reveal any neck or spine resistance. All reflexes were considered within the normal range. The rectal temperature was 100° F. Head and face pains had disappeared.

At 5:30 P.M. there was a return of the frontal and face pain, excruciatingly severe, which was relieved by ½ grain of codeine. At 11 P.M. neck resisted full flexion and was painful. Knee jerks were increased; the Kernig sign was positive; the ankle clonus was mildly positive; and the toe jerks were negative. The spinal fluid was turbid under moderate pressure. Several hours' search of smears showed gram-positive cocci in pairs and short chains, definitely encapsulated, morphologically *Streptococcus mucosus capsulatus* (Pneumococcus Type III).

The fluid was injected into a mouse and cultures were planted.

On Feb. 20, 1938, examination of the peritoneal washings from the mouse by the Neufeld method gave a positive reaction with Type III serum. Culture growth gave a positive reaction with Type III serum. It may be recorded here that smear, culture and mouse injection were negative for organisms on, and after, February 24 in every spinal fluid specimen until the first exacerbation in March.

TREATMENT

On admission, after three initial 5 gr. doses for tolerance, he was given 7½ gr. of sulfanilamide every four hours; and after the spinal fluid findings, concurrently with a dose of sulfanilamide, 10 c.c. prontosil was given intramuscularly, followed by 5 c.c. prontosil every four hours. Dosage is given in Table I.

In the hospital the Marshall method was used for sulfanilamide estimation. At the home the La Motte technique was employed.

TABLE I

DOSAGE*: FEBRUARY 19-25, 1938

SULFANILAMIDE				PRONTOSIL			
DATE	INTERVAL	DOSES	AMOUNT	DATE	INTERVAL	DOSES	AMOUNT
2/19	gr. 5.0 q4h	3	15	2/19	–		
2/20	gr. 7.5 q4h	10	75	2/20	10 c.c. stat	1	10
2/21	gr. 10.0 q4h	12	120	2/20	5 c.c. q4h	6	30
2/24	gr. 12.5 q4h	4	50	2/21	5 c.c. q6h	5	25
2/25	gr. 10.0 q8h	12	120	2/24	10 c.c. q4h	2	20
2/26	gr. 12.5 q8h	11	137.5	2/25	10 c.c. q6h	3	30
Totals		52	517.5			17	115

*Explanation of dosage tabulation:—The date is given when the various doses were started, and the actual doses given were counted until the order was changed. Where the doses are given in different amounts, every eight hours the doses are alternated. Therefore a dose is given every four hours.

Chart 1 shows a fairly typical temperature drop in less than 36 hours. However, it not only did not fall to normal but tended upward, a little down, and then irregularly to a higher level with wider variations. The leucocytes and neutrophiles followed the same curve.

Chart 2 shows the spinal cell count still at 2,400 on the fourth day.

OPERATION

As long as improvement justified it and until we could establish an acceptable blood concentration, we postponed an operation. However, at 8 P.M. February 24, operation was deemed wise. Under general anesthesia, a curvilinear auricular mastoid incision was made. The periosteum was elevated and the cortex removed with gouges. Diseased mastoid cells were found immediately under the cortex. The whole mastoid was seen to be diseased, with necrosis and breaking down of the intracellular septa. The cells were filled with a thick, gummy, sticky exudate. The tip was removed. A small area of dura over the lateral sinus was exposed. The sinus wall was normal. An area of dura over the middle fossa was exposed and was found to be covered with a granulation type of thick membrane. All of the dural plate was removed over the mastoid portion of the middle fossa and the dura was exposed over an area of about 3 cm. in diameter. All cells were clearly exenterated; the antrum was cleaned out; and the aditus was enlarged. A cigaret drain was inserted. The incision was closed with silkworm sutures and clips. The external auditory canal was packed.

FURTHER TREATMENT AND PROGRESS

Following operation 300 c.c. of citrated blood and 200 c.c. of normal saline were given by vein, and prontosil 10 c.c. were administered every four hours for two doses, and then every six hours for three doses. Sulfanilamide in doses of 12 gr. i ss,

TABLE II

DOSAGE: PERIOD FEBRUARY 26 TO MARCH 22, 1938

SULFANILAMIDE								TOTAL FORWARDED 517.5
DATE	INTERVAL	DOSES	AMOUNT	DATE	INTERVAL	DOSES	AMOUNT	
3/1	gr. 10.0 q4h	32	320.0	3/7	gr. 5.0 q8h	4	20	
3/6	gr. 7.5 q4h	7	52.5	3/8	gr. 5.0 q4h	24	120	
3/7	gr. 7.5 q8h	3	22.5	3/12	gr. 5.0 q4h	36	180	
	Totals	42	395.0			64	320	1232.5

alternating with 10 gr., was given every four hours, beginning at 7 A.M. February 25. On the same date 300 c.c. of 5 per cent glucose solution in saline was administered by vein at 8 A.M.

The wound filled in and closed with a minimum amount of drainage; and the patient was allowed to leave the hospital March 11, twenty days after admission.

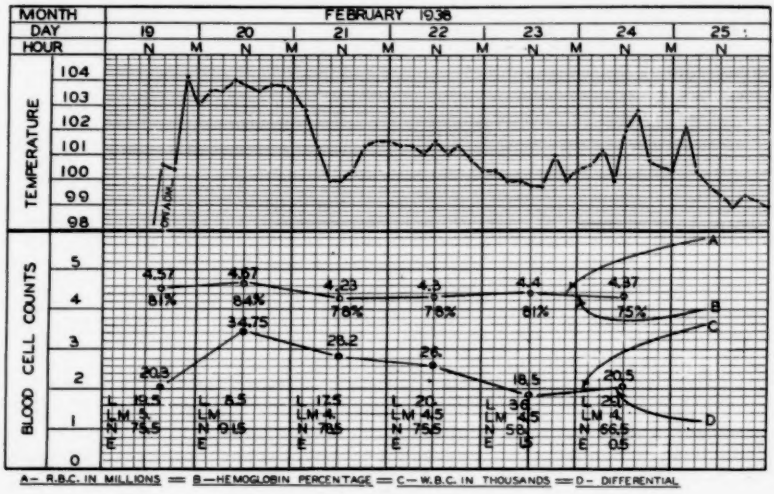


Chart 1.

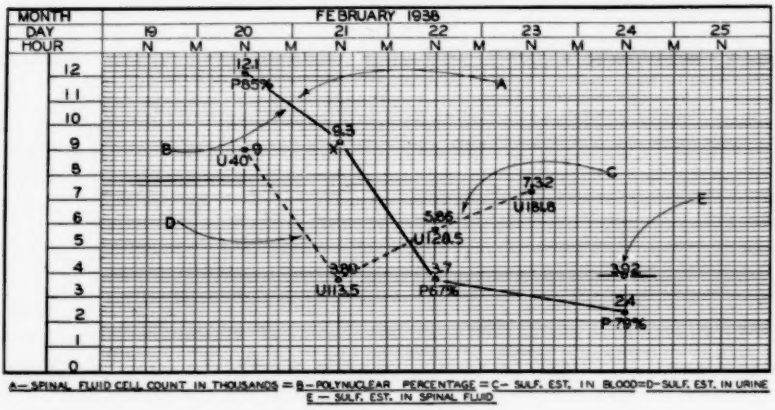


Chart 2.

After the operation he appeared sick but less toxic than our previous experience with meningitis would have led us to expect, and he tended to get better during his subsequent stay in the hospital and at home.

At home he ate well and gained in weight and strength. Gradually he was allowed to get up and out in a car. Blood concentration of sulfanilamide was 4 mg. His

leucocytes become normal, but the neutrophiles dropped so low that it alarmed us and the sulfanilamide was discontinued on March 18, when the neutrophiles were 28 per cent.

Chart 3 covers the time from the latter part of his stay in the hospital to his readmission.

Sulfanilamide dosage table shows drug administration for the period covered by Chart 3.

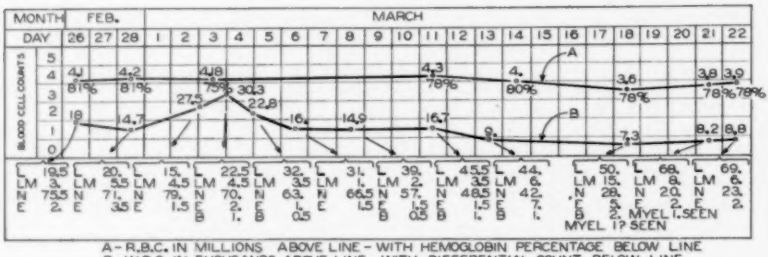
On March 24, three doses of prontosil, 10 c.c. each, were given intramuscularly at four-hour intervals.

TABLE III

DOSAGE: PERIOD MARCH 23-29, 1938

	SULFANILAMIDE						TOTAL FORWARDED 1232.5
DATE	INTERVAL	DOSES	AMOUNT	DATE	INTERVAL	DOSES	AMOUNT	
3/24	gr. 10.0 q4h	4	40.0	3/27	gr. 12.5 q8h	3	37.5	
3/25	gr. 12.5 q4h	13	162.5	3/28	gr. 7.5 q8h	10	75.0	
3/27	gr. 10.0 q8h	4	40.0	3/28	gr. 10.0 q8h	9	90.0	
	Totals	21	242.5			22	202.5	1677.5

Forty-eight hours after the drug was stopped he came in from play in the afternoon very tired. The following day this was much more in evidence. The next day he preferred to remain in bed. On the fifth day he was admitted to the hospital. His temperature continued normal. There was no pain. General examination was negative

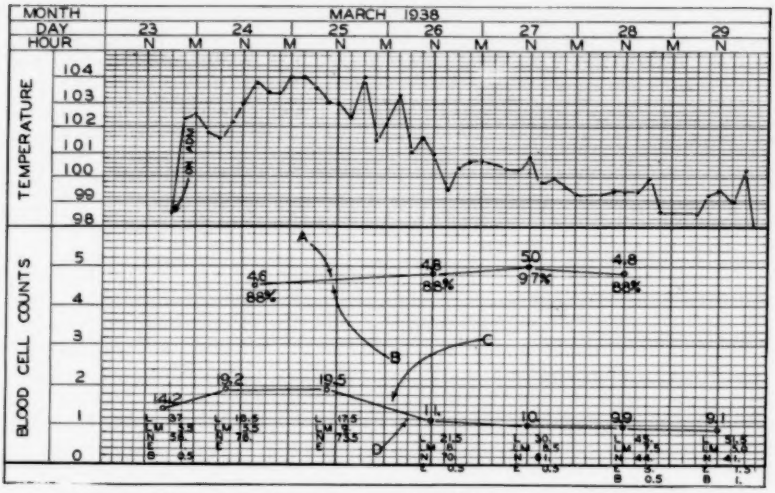


A-R.B.C. IN MILLIONS ABOVE LINE-WITH HEMOGLOBIN PERCENTAGE BELOW LINE
B-W.B.C. IN THOUSANDS ABOVE LINE-WITH DIFFERENTIAL COUNT BELOW LINE

Chart 3.

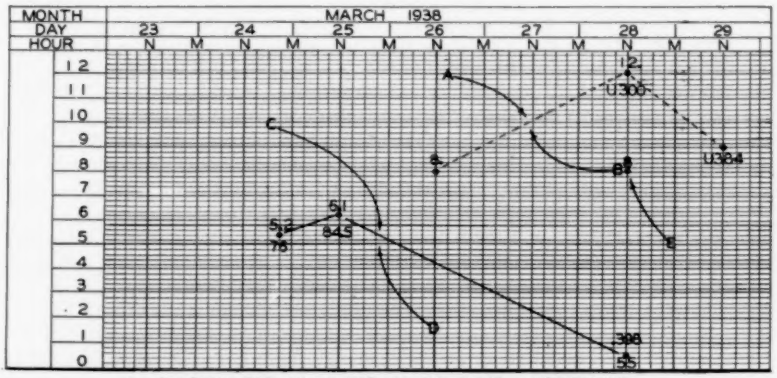
He was readmitted to the hospital on March 23, and, with the hope that it would stimulate the boy and the neutrophiles, the same donor as previously employed was used for a 250 c.c. blood transfusion. His anemia was not marked but was sufficient to justify a small transfusion. His face was flushed in an hour after transfusion and his temperature, as shown in Chart 4, was stepped up. We thought at first it might be due to a reaction to transfusion, but the following afternoon spinal puncture showed a slightly turbid fluid.

Since the reinfection response of the white cells and the differential count were within limits of normal expectation and the cell granules continued to stain normally and with less fear of a distinct, but not increasing, cyanosis of the lips and duskiness of the skin, we began then to use a larger dose of sulfanilamide and maintain a somewhat higher level of concentration in the belief that the drug would be



A - R.B.C. IN MILLIONS ABOVE LINE- B-HEMOGLOBIN PERCENTAGE BELOW LINE
C - W.B.C. IN THOUSANDS ABOVE LINE- D-DIFFERENTIAL COUNT BELOW LINE

Chart 4.



A - SULFANIL. EST. IN MG. PER 100 C.C.-BLOOD - ABOVE LINE
B - SULFANIL. EST. IN MG. PER 100 C.C.-URINE - BELOW LINE
C - SPINAL FLUID CELL COUNT IN THOUSANDS ABOVE LINE
D - POLYNUCLEAR CELL COUNT BELOW LINE
E - SULFANIL. EST. IN MG. PER 100 C.C. OF SPINAL FLUID

Chart 5.

less effective during relapse of the disease. The relapse and the original curve of the infection were quite similar, except that the temperature's return to normal was a little slower. The boy seemed to be as ill in the relapse as he was in the original attack.

The examination of the spinal fluid:

March 24, smears of the spinal fluid showed no organisms.

Spinal fluid was injected into a mouse with no apparent ill effect.

Cultures of the spinal fluid showed no growth.

March 25, smears of the spinal fluid showed no organisms.

A second spinal fluid was injected into the same mouse which was used on March 24. The mouse was killed after twenty-four hours. No organisms were found in the peritoneal washings.

Cultures of the spinal fluid of that date showed a few gram-positive cocci after forty-eight hours. This was injected into a mouse. Examination of the peritoneal washings from the mouse by the Neufeld method showed a positive reaction with Type III serum.

Sedimentation rate:

March 24,	sedimentation rate	16 mm. per hour
	cell volume	45 mm.
	corrected rate	14 mm. per hour
	(Wintrobe method—normal for males—up to 9 mm. per hour)	
March 26,	sedimentation rate	25 mm. per hour
	cell volume	45 mm.
	corrected rate	22 mm. per hour
	(Wintrobe method—normal for males—up to 9 mm. per hour)	

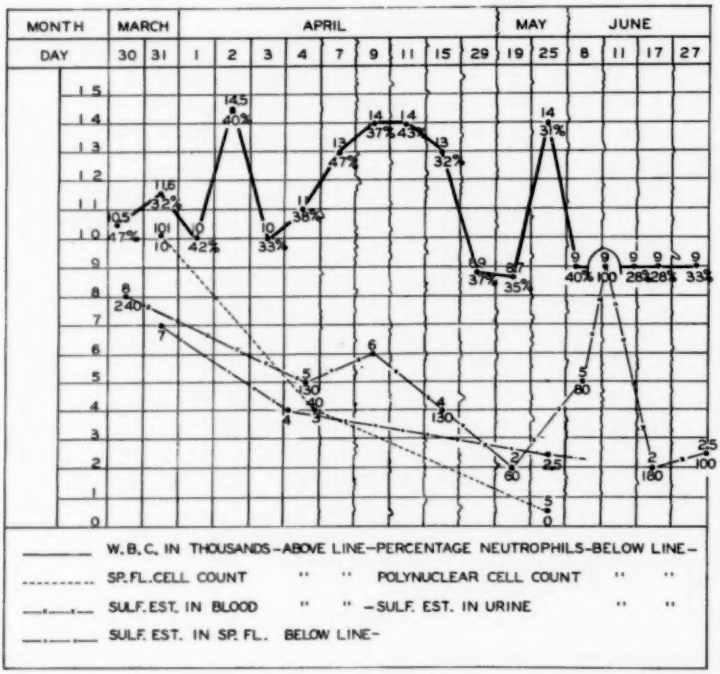

MONTH
MARCH
APRIL
MAY
JUNE
DAY
30 31 1 2 3 4 7 9 11 15 29 19 25 8 11 17 27
W.B.C. IN THOUSANDS-ABOVE LINE-PERCENTAGE NEUTROPHILS-BELOW LINE-
SP. FL. CELL COUNT " " POLYNUCLEAR CELL COUNT " "
SULF. EST. IN BLOOD " " -SULF. EST. IN URINE " "
SULF. EST. IN SP. FL. BELOW LINE-

Chart 6.

With the control of acute symptoms of the relapse, the white cells dropped to lower level with a subnormal neutrophile percentage. Because of past allergic manifestations, we began powdered liver extract with iron (Lilly No. 55) rather than hypodermic administration. Beginning April 3, one teaspoonful three times a day was given continuously with the exception of the period of June 12 to 18. It was finally stopped when all medication was discontinued on June 26.

After that the temperature returned to normal. The remainder of the months of March, April, May and June are summarized in Chart 6 which covers a period spent partly in the hospital and partly at home with a trained nurse. During that time there were two intervals of distinct relapse. The recovery from neither seemed complete.

On May 22, the temperature was up to 100.2° F. over a period of four days, with a slight elevation in leucocyte count. There were periods of frequent pains in the frontal region and in the side of the face. He preferred to stay in bed rather than get up. Sulfanilamide was increased from 5 gr. to 7½ gr. doses; and after about a week he was permitted to get up again.

A second very similar attack with a temperature at 100.2° F. occurred on June 8, with additional symptoms. He complained of tingling in his mouth and pain in the right side of his neck and some very doubtful pain in the right leg. The sulfanilamide was increased to 10 gr. every four hours and was held at that for four or five days. In neither of those attacks did he show neck resistance or changes in his reflexes. His blood concentration was carried up to 9 mg. per 100 c.c.

In Chart 6 the total white count is given above the line, and the per cent of neutrophiles below the line. At times there were slight variations in eosinophiles and mononuclears, but they were never more than moderately increased and at no time during the course of the illness was there any difference in the therapy because of their variation. The full differential was omitted for the sake of clearness.

A study of Chart 6 shows that from March 30 to June 11 there was a tendency for the leucocytes to stay above normal. After neither of the above relapses did he impress one as returning to normal; and for that reason he was returned to the hospital June 11. From a new donor, 200 c.c. of citrated blood followed by 200 c.c. normal saline was given. Following this, the count did remain normal, and the boy appeared normal. All medication was stopped June 26; the nurse was permitted to go; and the patient was finally discharged on July 1.

TABLE IV

DOSAGE: PERIOD MARCH 30 TO JUNE 26, 1938

	SULFANILAMIDE							TOTAL FORWARDED 1677.5
DATE	INTERVAL	DOSES	AMOUNT	DATE	INTERVAL	DOSES	AMOUNT	
3/30	gr. 7.5 q4h	5	37.5	5/22	gr. 5.0 q8h	3	15.0	
4/1	gr. 5.0 q8h	13	65.0	5/24	gr. 5.0 q4h	8	40.0	
4/1	gr. 7.5 q8h	13	97.5	5/25	gr. 7.5 q4h	29	217.5	
4/5	gr. 5.0 q4h	11	55.0	5/31	gr. 5.0 q8h	14	70.0	
4/7	gr. 7.5 q4h	19	142.5	5/31	gr. 7.5 q8h	16	120.0	
4/10	gr. 5.0 q4h	76	380.0	6/6	gr. 5.0 q4h	7	35.0	
4/23	gr. 7.5 q6h	25	187.5	6/6	gr. 12.5	1	12.5	
4/29	gr. 5.0 q6h	81	405.0	6/7	gr. 10.0 q4h	24	240.0	
5/19	gr. 5.0 q4h	19	95.0	6/12	gr. 7.5 q6h	3	22.5	
5/22	gr. 7.5 q8h	3	22.5	6/13	gr. 5.0 q6h	45	225.0	
	Totals	265	1487.5			150	997.5	4162.5

Total period: February 19 to June 26, 1938
Doses prontosil 20—145 c.c.
Doses sulfanilamide 616—270.3 gm.

SUMMARY

From the admission to the hospital on February 19 to June 11, there never was a time when there was any doubt that the patient's recovery was incomplete. After the latter date he appeared to get well rapidly and to maintain his well-being.

When sulfanilamide was discontinued on March 18, it was very impressive that rapidly, in approximately forty hours, his symptoms became progressively worse, so that on the fifth day he suffered a severe exacerbation of symptoms. His symptoms reappeared at about the time necessary to eliminate the sulfanilamide.

The third relapse responded to treatment unsatisfactorily and was followed by a more pronounced relapse in a short time. More energetic treatment and a third transfusion instituted the beginning of recovery.

It is most impressive that in his March hospitalization the severity of the illness indicated an organism at least as virulent in the primary sickness; yet the organism was recovered with difficulty. Never at any time did any of the mice give clinical signs of being ill after inoculation, and the organism did not grow readily in culture media.

Sulfanilamide did not destroy this organism; and, while its virulency to mice and its cultural growth seemed very much affected, at the same time its power to overwhelm the patient seemed unimpaired after a month of controlling administration of the dye. Certainly the development of immunity seemed to be nil, or exceedingly slow.

Nausea at times, particularly after the relapse of March 23, necessitated temporary reductions of the sulfanilamide dosage. Bicarbonate of soda, 10 grains, three times daily, or 5 grains with larger doses, seemed to reduce upsets.

Anemia was mild throughout—just sufficient to justify small stimulating transfusions. The response to transfusion of June 11 was most pleasing.

During the entire course the spinal fluid pressure was not excessive. Only once with an air manometer did it reach 340 mm. The use of the manometer was discontinued after several repetitions because of evidence of low pressure and, particularly, because the manipulations tended to increase the contamination of spinal fluid specimen with blood cells.

After our experience in the March flare-up we planned to continue therapy until the evidence of recovery should include not only normal general symptoms, temperature, white blood counts and differentials, but if possible also a spinal fluid within a normal range. The spinal fluid cell count was normal on May 25 and after June 11. We did not consider another spinal puncture was justified.

The healing and filling in of the mastoid wound approached as nearly as was possible a primary healing. With the immediate operative field apparently out of the picture, the pneumonic exudate on the meninges must have been the focus of infection from which reinfections came.

Hewell and Mitchell[1] report recovery in two cases of pneumococcic meningitis, Type III, with sulfanilamide compounds. In both cases ethylhydrocupreine hydrochloride was given. Their review of the literature adds three more cases of recovery.

One of their patients had exacerbations, and the recovery followed trepanation and aspiration of pus from the right temporal region.

This case is unique in that it is the only recorded instance of recovery we could find in our review of the literature in which recovery followed repeated relapses. The duration both of the disease and of the administration of sulfanilamide is unusual.

The boy's weight on February 5, before onset, was 69 pounds 4 ounces. His weight on July 1 suggested a very appreciable gain; and on December 2 was 89 pounds. Seven months after recovery he was fully within normal both physically and mentally.

Throughout the entire illness Dr. Henry F. Martin was in charge of the ear therapy, including all operative procedures.

Grateful acknowledgment is here made to Dr. Perrin H. Long, of Baltimore, for his comforting and helpful advice in repeated telephone consultations. His aid and the interest of the other consultants are deeply appreciated.

REFERENCE

1. Hewell and Mitchell: J. A. M. A. **112**: 1033, 1939.

LOCALIZED ACUTE ENTERITIS WITH PERFORATION AND PERITONITIS

Report of a Case in a Five-Day-Old Infant

Charles Barnum, M.D., and Maurice R. Moore, M.D., C.M.
New London, Conn.

IT IS our desire to place on record a case of a newborn infant who developed abdominal distention when 30 hours old, a temperature of 101.2° F. at 57½ hours, and died on the fifth day.

The mother, Mrs. R., was a 26-year-old para iii, with two living healthy children. She had a normal spontaneous delivery, of right occiput transverse, fourteen days before the expected date, and the puerperium was afebrile. There had been no recent history of illness.

The baby, a girl, was born May 30, 1938, and died June 3, 1938. The baby cried spontaneously. A stethoscopic examination of the heart and lungs at birth showed no abnormalities. Bilateral parietal cephalematoma of moderate size gradually developed during the first twenty-four hours after delivery.

On June 1, at 10 A.M., the abdomen was found markedly distended. A colonic irrigation was given which returned with unsatisfactory results and appeared to contain some bile. Citrated maternal blood, 20 c.c., was given intramuscularly. About 6 P.M., the doctor was called because of the abdominal distention, and he found the physical examination negative except for the cephalematoma and the distention.

On June 2, the extremities were found cold, the baby dehydrated, and the abdomen markedly distended. A colonic irrigation returned with a large amount of stool, the latter part of which was yellow in appearance. Two doses of pitressin, each of 2 minims, were given, and a quantity of gas was expelled with some relief of the distention. The baby appeared weak although it had nursed and taken formula well up to that time.

On June 3, the distention had returned. The infant's heart rate was very rapid. There was a rough systolic murmur in the region of the left breast. The lungs were clear. The baby died June 3 at 5 A.M.

At autopsy the abdomen was markedly distended. On incising the peritoneum, gas was found to escape in relatively large quantities. A great number of plastic adhesions and moderate quantities of yellowish fluid were found throughout the greater peritoneal sac. The ileum, at points diametrically opposite the mesenteric attachment in the region of Peyer's patches, approximately 7.5 cm. and again 30 cm. above the ileocecal junction, showed areas of the mucosa ulcerated, and there was fibrinous exudate on the external surface. The more distal lesion was perforated. Normal yellow stool was escaping through the perforation. The lumen of the large bowel contained considerable mucus, clear in color. The rectum had areas of congestion in its mucosa. The other parts of the gastrointestinal tract and the rest of the body were essentially negative.

Microscopic examination added no information to the gross findings.

From the Lawrence and Memorial Associated Hospitals, New London, Conn.

An aerobic culture was made from the peritoneum which showed a pure growth of bacilli with the following characteristics: Gram-negative, nonmotile bacillus; colony on blood agar, smooth, large and grayish with a mucoid appearance. In sugar: acid and gas in dextrose, maltose, mannite, lactose. Negative in sucrose. Nitrates reduced to nitrites. Indol formed. Litmus milk coagulated. No anaerobic culture was made.

In recent years a number of articles on diarrhea in the newborn have appeared in literature; much work has been done which is still to be reported. There has been no identification of a single etiological agent responsible for the epidemics. The most consistent bacteriologic finding has been a gram-negative organism resembling the Friedländer's bacillus appearing in the stools of the patients. The action of these bacteria is difficult to understand because of their close relationship to some soil, nonpathogenic germs.

The case here reported would forcibly indicate a definite etiological relationship between the bacillus present in pure culture in the peritoneal cavity and the ileitis with perforation and peritonitis.

SUMMARY

1. The inflammatory areas of the ileum were remarkable because of the extensive necrosis and small amount of exudate.

2. The organism found in pure culture in the peritoneal cavity falls into the genus aerobacter, aerogenesis group.

REFERENCES

1. Pool, M. W., and Cooley, T. B.: Am. J. Dis. Child. **43**: 1101, 1932.
2. Durand, J. T.: J. PEDIAT. **7**: 1935.
3. McKinlay, B.: Am. J. Dis. Child. **54**: 1252, 1937.
4. Frant, S., and Abramson, H.: J. PEDIAT. **11**: 772, 1937.
5. Rice, J. L., Best, W. H., Frant, S., and Abramson, H.: J. A. M. A. **109**: 475, 1937.
6. Ludlum, W. D.: J. A. M. A. **110**: 23, 1938.
7. Bundersen, H.: J. A. M. A. **110**: 16, 1938.
8. Best, W. H.: J. A. M. A. **110**: 15, 1938.

A SIMPLIFIED METHOD FOR SCALP VEIN TRANSFUSIONS IN INFANTS

SIDNEY A. KAUFFMAN, M.D., AND SIDNEY O. LEVINSON, M.D.
CHICAGO, ILL.

THE value of intravenous fluids and blood in acute infections and nutritional disturbances in infants and children is reflected in the increasing use of these agents in treatment. This fact becomes obvious when one considers the frequency with which this therapeutic measure is employed in a modern pediatric hospital. During the development of this replacement therapy in pediatrics in the past two or three decades, various routes such as subcutaneous, intramuscular, and intraperitoneal have been employed in preference to intravenous administration. These other routes were not employed because they were superior, but because they avoided the technical difficulties encountered in attempting intravenous infusions. These difficulties were chiefly due to the small caliber of veins and the failure to retain the needle in the vein long enough to administer any large volume of blood or fluid.

The veins available for venipuncture in an infant are the longitudinal sinus, the jugular, scalp, arm, and ankle veins. The longitudinal sinus has usually been employed as a last resort. The jugular, scalp, and arm veins never achieved any degree of popularity because of the difficulties mentioned above. The ankle vein was used even less than the other veins, until the technique for exposing and cannulating this vein was perfected and simplified by Spivek.[1] This method so facilitated the procedure that ankle vein infusions and transfusions have become very common. Frequent objections raised to this method have been that it required a skin incision, with its potential danger of infection, and the likely loss of the vein either through thrombosis or ligation, as is frequently done. This latter objection is particularly serious in cases of sepsis or anemia requiring repeated transfusions and where an available supply of veins must be maintained. Despite these objections, the "cut-down" technique is without equal in its simplicity, particularly in patients requiring continuous and prolonged fluid and blood administration.

In certain sections scalp vein puncture has been employed in preference to the "cut-down" method for repeated small infusions and transfusions. This preference was based on the fact that it obviated

From the Sarah Morris Hospital and the Samuel Deutsch Serum Center, Michael Reese Hospital.

the objections to the "cut-down" method and, in addition, spared the ankle veins as an excellent reserve. Moreover, many dehydrated infants can be sustained by a combination of subcutaneous and of small repeated scalp vein infusions until adequate oral intake is reached.

However, there are certain difficulties in the use of the scalp vein technique, which limit its practicability and resultant widespread use. The scalp veins are small, not only requiring but necessitating a very small caliber needle. As a result, gravity flow is usually unsuccessful, and some method of injection is needed. It is almost impossible to use the direct syringe-needle method, because the slightest movement of the child's head causes the needle to slip out of the vein. Ormiston[2] stressed the value of using the scalp veins for continuous intravenous administration, relying on gravity for the fluid infusion. Although glucose or saline may be given by gravity flow for a short time, it has been our experience that this method is successful only with the large size scalp veins and is quite unsatisfactory for transfusion of blood or for application in the usual small veins where small caliber needles are required.

One of us (S. A. K.) is familiar with the method used in several Eastern hospitals, consisting of a three-way stopcock side-arm double syringe burette outfit. The infusion of blood is accomplished through an injection syringe attached to the system by a Y-tube at a distance from the scalp needle. An assistant operates the Y-tube syringe by multiple aspirations from the burette and injection into the tube leading to the vein. In this way minor movements of the infant's head do not cause the needle to slip from the vein. This apparatus requires skillful manipulation to work successfully and has the following drawbacks: (1) many items of equipment with their attendant expense and breakage; (2) great care necessary to maintain airtight glass-rubber junctions; (3) time consumed in cleaning, assembling, and sterilizing many parts; (4) necessity of an additional assistant to operate the aspiration-injection syringe. These complications have prevented the scalp vein technique from attaining any general use.

In order to simplify the scalp vein route for transfusion so that it becomes practical, we have adopted the "milking tube" device to pump the blood into the scalp vein. This principle was originally designed for direct transfusions.[3, 4] The apparatus described by C. M. Van Allen[5] was most applicable for our work, but had to be modified in several ways (Fig. 1). We employ a three-roller wheel. A curved metal band serves as a bed for the rubber tubing of the administration set, and the bed is hinged to a central metal shaft by a pin permitting a rocking movement of the bed, which both maintains contact be-

tween the tubing and the moving rollers at a constant maximum compression and avoids creeping of the rubber tubing. The central metal shaft supporting the bed moves in a vertical direction in a sleeve. A strong metal spring at the bottom of the sleeve imparts constant upward pressure. To adjust the rubber tubing in place, the bed system is pushed down and held in a lowered position by engaging with a catch (Fig. 2). After the tubing is placed in the bed, the catch is released and the spring raises the bed into apposition with the rollers (Fig. 3).

The speed of the central wheel is decreased by means of a reduction gear so that the ratio of the rotating handle and central wheel is 7 to 1. This permits a comfortable rate of speed in turning the operating handle (20-30 per minute) and avoids too rapid injection of fluid.

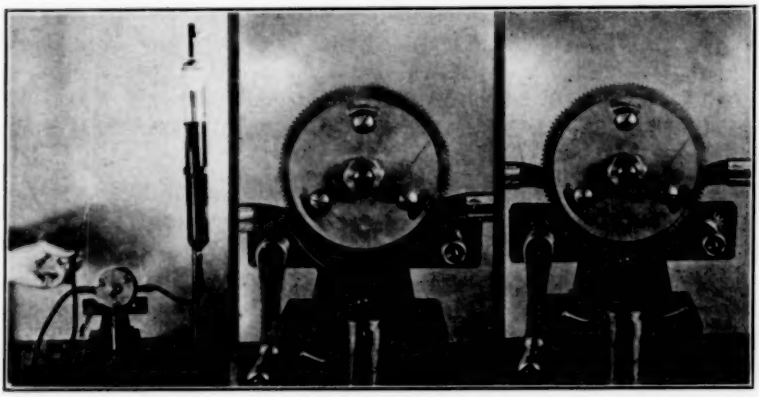


Fig. 1. Fig. 2. Fig. 3.

The only equipment that must be assembled and sterilized, as shown in Fig. 1, is a 250 c.c. burette, with a cotton gauze stopper, about two feet of transparent rubber tubing, glass adapter, and scalp needle.

When a transfusion is to be given, the burette is suspended from the vertical rod. The rubber tubing is placed in the bed of the machine and the catch is released. This brings the tubing in apposition with, and compression by, the rollers (Fig. 3). A small amount of sterile physiologic saline is poured into the burette, and several turns of the handle fills the system with the saline. The citrated and filtered blood to be administered is then poured into the burette, which is capped with a gauze stopper. After the infant is immobilized in a blanket, his head is shaved and prepared with iodine and alcohol over the temporal region. A nurse holds the infant's head firmly and with her thumb compresses the superficial temporal vein anteriorly to the tragus of the ear. Friction with a sponge and tapping usually makes the vein sufficiently prominent. The needle is inserted into the

vein in a caudad direction. Blood usually appears in the glass adapter as soon as the needle penetrates the vein. If this does not occur, a one-half reverse turn of the handle of the apparatus produces enough suction to aspirate blood into the glass adapter, although blood may not be withdrawn from a very small vein. Once the needle has been inserted into the vein, it is easily held in place by the index finger of the left hand over the needle, and movements of the head do not dislocate the needle from the vein. The handle of the machine is then turned with the right hand at a comfortable rate (about 30 revolutions per minute) which results in an infusion rate of from 10 to 15 c.c. per minute. This rate may be varied at will.

We have found that the use of this instrument does away with the labor and difficulties of the syringe method and facilitates the introduction of fluids by the scalp vein route. A 23 gauge 1¼ inch long needle with a short bevel is best adapted for scalp venipuncture, although with this method long hypodermic needles (26 to 27 gauge, 1 inch long) may be successfully used for very small veins.

As Van Allen has pointed out, this instrument lends itself for other uses where suction or pressure is necessary. We have employed it in situations where, in the past, multiple syringes have been required, e.g., administration of large quantities of serum, gum acacia, etc.

SUMMARY

1. Various routes for intravenous administration of fluids and blood in infants are discussed.

2. The advantages and disadvantages of the scalp vein method are considered.

3. The scalp vein technique is simplified and facilitated by use of a modification of the roller pressure apparatus.

REFERENCES

1. Spivek, M. L.: J. Pediat. **7**: 199, 1935.
2. Ormiston, George: Lancet **1**: 82, 1938.
3. Beck, A.: Ergebn. d. inn. Med. u. Kinderh. **30**: 150, 1926.
4. De Bakey, M.: New Orleans M. & S. J. **87**: 386, 1934.
5. Van Allen, C. M.: J. A. M. A. **98**: 1805, 1932.

Special Article

THE ROLE OF GRATIFICATION IN EARLY DEVELOPMENT

C. Anderson Aldrich, M.D.
Winnetka, Ill.

THE title of this article might as properly have been "The Role of Positive Conditioning in Early Development." Its present wording is given, however, because it expresses more nearly the viewpoint of a clinical observer rather than that of a psychologist, neurologist, or anatomist. And since pediatrists comprise, perhaps, the only professional group who ordinarily have an opportunity to observe numbers of babies over long periods of time, such observations as they may make have a certain practical interest for those who, by the nature of their work, do not come into such close contact with young infants.

In order to orient ourselves, I would like to review, for a few moments, the earlier processes of growth. In thinking of newborn infants, we must remember that they are, in reality, by no means new, for at birth they represent not only the result of human evolutionary progress but also the summation of all the preparation which has gone on during intrauterine existence. The baby has been preparing adequate cardiovascular, glandular, gastrointestinal, and other vital functions during this time, as well as developing the reflexes and behavior patterns which he will find necessary for immediate use after he is born. And, in many instances, these abilities have been tried out and exercised within the uterus before independent living begins.

Thus we find that the baby comes into the world as a well-organized individual, equipped with the absolutely necessary tools for living and functioning largely on a reflex or subcortical basis. His apparatus, at birth, includes the internal controls over vital functions which we have mentioned, as well as the ability to adjust to rapid growth with precise and accurate synchrony. In addition, he has the more obvious reflexes and behavior patterns which govern respiratory, nursing, and postural functions. Much of this reflex equipment comes under the head of defense mechanism, the startle, withdrawal, and blinking reflexes, the shiver, the cry, and his resistance to restraint. The serious, compulsive, self-protecting character of the newborn baby is impressive to observe, as he defends himself by every means in his power against cold, hunger, restraint, and pain.

Read before the American Academy of Pediatrics, Region II, Oklahoma City, Okla., Nov. 16, 1938.
Approved by the Committee on Mental Hygiene, American Academy of Pediatrics.

The developmental plan of maturation operates as a series of progressive changes in which all parts of the body increase in size and improve in function. Form and function are inseparable in orderly growth. These complex activities proceed in a severely regimented sequence, although considerable latitude is allowed as to rate. The developmental plan by which growth takes place allows for the gradual elevation to a conscious level of two opposite functions, the sensory or receiving function and the motor or outgoing function. And the baby's behavior, when it reaches this conscious level, will depend largely upon the type of early experience he has had. Since this is so, we cannot have perspective on his development without taking into account the immediate action of this environmental experience on his maturation processes. For, from the beginning, the growth plan is set up in such a way as to require that a harmonious environment supplement its activities, if it is to work efficiently and safely for the child.

Many of the environmental needs of the infant have long been recognized in our modern routines for children. Fresh air, sunshine, adequate clothing, food, and sleep are among the approved satisfactions which are conscientiously provided and are a part of our program for nursery care. But there are other needs which any thoughtful observer must come to recognize as equally important. The warmth and contact of the mother in the first few weeks, the security of fondling, freedom from physical restraint, permission to eat, sleep, and eliminate according to his own individual rhythms rather than by those imposed by arbitrary regimes, the opportunity to try out and use his emerging activities as they appear within the developmental plan, these also may be considered as positive requirements. And it is the purpose of this paper to call attention to the fact that when such needs are considered and are generously satisfied, we collaborate with the growth plan, and that when they are minimized or ignored, growth is hampered and warped. In other words, the gratification which the baby gets from the fulfillment of these needs is the spark which makes the developmental plan work at its maximum efficiency. It is back here, in the comparatively simple performance of the earliest days of life, that the child begins to develop the positive conditioning and the sense of competency which we recognize as so important for the later success of the individual.

I know of no better place to illustrate how gratification assists the growth process than in the feeding activities of the infant. The feeding behavior of the young baby can be said to grow by the progressive elevation of simple reflexes to more complicated reactions under cortical control, so that an act which is in the beginning involuntary, comes gradually under the complete mastery of volition. Feeding behavior also grows through the emergence of more and more complicated behavior patterns, as the developmental plan matures.

The most primitive form of such behavior is the hunger contraction, which takes place in the muscular wall of the stomach of the newborn baby. This is, as far as we know, a result of factors residing only in the organ responding. The simple act, however, results in the hunger cry of distress, rooting movements of the head, hand-to-mouth activity, and, under proper conditions, swallowing—a series of reflex activities which involves participation of spinal nerves.

From this point, feeding goes on to function at higher levels, as the more complicated patterns which are included in the eating picture begin to emerge. At this point, too, gratification becomes a factor, for the baby, under the influence of violent hunger pains, is placed in his mother's arms where he is warmed and soothed by this contact, and his pains are immediately relieved as soon as any fluid touches the inside of his stomach. The sudden stopping of pain is a gratifying experience, the warmth is pleasant, and he is allowed, in the process of nursing, to exercise the whole gamut of feeding activities with which he is at that time endowed, the rooting movements in search of the nipple, suckling, and swallowing. Thus we can see that the pleasures of nursing result from the satisfaction which comes from the exercise of emerging powers, as well as from the relief of pain and from warmth.

After a few experiences of this sort, the entire nursing process becomes positively conditioned. Every pediatrist is familiar with the sighing, guzzling sounds that very young infants make to register their enjoyment of nursing. This very process raises the feeding act above the level of a simple cord reflex, as emotional factors exert their influence. Thus, eating is stepped up a plane, although it may still be partly subcortical. Later on, under favorable circumstances, the baby learns that more varied foods lead to this same sort of gratification of his needs and begins to look forward consciously to the enjoyment of meals. Again, feeding is elevated to the still higher levels of purposeful behavior. At these upper levels the psychic mechanism which is a part of appetite is recognizable, and the child voluntarily likes to eat even when not under the compulsion of his ancient and obscure hunger cramps. During his early months the development of the motor patterns of hand and arm are devised to give him a sense of competency and enjoyment in his feeding situations. A baby's determined efforts to feed himself as soon as he is able are a part of his growth requirements. He reaches out greedily to grasp the bottle as soon as his hands can accomplish this feat, and when he becomes more expert, he enjoys using the spoon himself. In fact, we sometimes see infants who insist so violently on being allowed to feed themselves that they will knock the spoon out of the hand of anyone who tries to feed them.

If the above illustration shows the many places at which gratifying experience helps the baby to improve his complicated feeding processes,

we must remember also that at each such place there are equal possibilities that the opposite sort of conditioning may occur, tending to block his progress. In this way we can explain many forms of anorexia, children who refuse to be weaned from breast to bottle, from bottle to cup, and who will not go on to feed themselves. It would be interesting, if time permitted, to study such obstructions.

But in this discussion it is more to the point to show that all of the baby's growing abilities are elaborated from simple reflex or behavior pattern cores to complicated, voluntary acts by this same beneficent process of gratifying experience. Thus, the evacuation of the bowels begins as a simple organ reflex under the compulsion of the mass movement. As the infant learns by experience that the discomfort of rectal distention is relieved by the muscular effort of elimination, the act becomes pleasant, positively conditioned, and later on under favorable circumstances comes under voluntary control as one of life's agreeable sensations. The same sort of progress happens in the growth of urinary control.

We find a similar mechanism at work in the attainment of motor control. In learning to use his hands, for instance, the baby, at first, is capable only of random movements, the reflex grasp, and such behavior patterns as the Moro and tonic neck reflexes. As he grows, he becomes interested through vision in the behavior of these queerly waving appendages and quite evidently gets a great deal of satisfaction in his increasing control over their movements. Smiles and crows attest his triumph as he persists in his practice at hand manipulation, until eventually he will be able to perform with great dexterity all the acts called for in adult life. And all the way along, satisfaction is spurring him on to more adequate performance.

I do not have to point out that the modern care of babies has, in its application of rigid routines, tended to oppose such natural progress. We find that individual rhythms are often ignored in our so-called "training" of eating, sleeping, and eliminating, that many physical activities are restrained, and that we place unnecessary restrictions around a child's growing capacity for motor accomplishment, crawling, standing, and walking.

Moreover, we often hear it said that to comfort and cuddle the baby is disturbing to his routine and softening to his character. Some of our enthusiasm for this Spartan treatment has naturally grown up because of our fear of "spoiling" the child. It has been my experience, however, that spoiled children are not usually those who have been given these requirements, but are instead those whose essential satisfactions have been curtailed in a mistaken effort to make them conform to a rigid routine. Children who lack the fundamental security which these early gratifying experiences give are likely to compensate by attention-getting devices of whining and tantrums and in this way to develop the disagree-

able personality of the "spoiled child." Satisfied children, on the other hand, do not need to develop such unpleasant techniques and so are more amenable to adult suggestion.

Much of our thwarting, however, has taken place in the interests of what we call "good" or regular habits. We are inclined to lose sight of the fact that the baby is a dynamic organism who has within him the capacity for his own regular habits. It might be timely, at this point, to refer to common, natural phenomena, for the purpose of observing the rhythm and regularity of nature. The days and the seasons, the migration of birds, the hibernation of animals, the ripening of grain, the menstrual cycle, many fundamental, natural processes display this infallible regularity. Those who daily observe human infants cannot fail to see in them this same sort of behavior. The growth plan is inexorable in its sequence, and the functions important to growth must and do carry on in a regular or rhythmic way. The interval between feedings tends to become exact, the timing of bowel and bladder evacuations tends to become more and more accurate with elapsing weeks. The relation between sleep and waking hours changes progressively and similarly in practically all babies, if their own regime is not interfered with.

Are we really, then, concerned about the formation of regular habits, since we know the tremendous urge to regularity which is built into their specifications? It seems to me that the problem is not one of regularity but rather that, in many instances, the baby's own regime does not entirely synchronize with his environment, with the complicated, daily schedule of our civilized life. The issue, at least in respect to the habit formation of the physical functions of the infant, is one of adjustment between two familiar forces, natural growth and civilized environment. It is not the purpose of this paper to decide to what extent either should be favored. Certainly, in many ways, it is as important that a child learn to conform to his world as it is that he grow up. I am merely trying to call attention to the fact that in the smooth functioning of the developmental plan of growth, the fulfillment of fundamental needs, gratification if you will, plays an important, positive role; and that in our attention to the fields of habit-training and schedule, we are bound to take into account the importance of these needs of growth and to modify our techniques accordingly. To those whose work lies with children such modifications open a wide field of interest, not only for the pediatric profession, but also for those who are concerned with education and with what, for lack of more accurate name, we call mental hygiene.

Critical Review

INFANTILE SEXUALITY

LEO KANNER, M.D.
BALTIMORE, MD.

SEX development and sex behavior during childhood have received little, if any, attention in pediatric literature.

Embryologists have studied the fetal evolution of the organs destined to serve the purpose of procreation. Anatomists have described the macroscopic and histologic characteristics of these organs in the successive years between birth and adolescence. Physiologists have interested themselves in the earliest stages of ovulation and menstruation in the female and ejaculation and composition of the spermatic substance in the male. Clinicians and pathologists have been led by various, in the whole infrequent, syndromes to explore the relationship between the endocrines and devious, precocious or retarded, development of the genitalia and their functions. Pediatricians have occasionally been reminded of the sex organs of children by the finding of undescended testicles, phimosis, balanitis, gonorrheal or unspecific vaginitis, and some of the more unusual diseases and anomalies of the genitalia. These conditions were treated locally and for the most part indeed required no other consideration.

Apart from that, "sex" was regarded by physicians and the laity alike as something that was blissfully nonexistent or latent until puberty, when somatic changes were believed to direct an hypothetical sex instinct more or less abruptly towards romance and mating. It was taken for granted that all other propensities of the species—somatic growth, cognition, physiognomic, postural, oral and graphic symbolization, locomotor and adaptive reaching out into the environment—undergo gradual expansion from the beginning of life. Yet the procreative potentialities and their psychobiologic, attitudinal and behavioral implications were somehow assumed to be dormant, if not altogether absent, during the first decade. Children were looked upon categorically as asexual beings. This fiction of angelic innocence was to be preserved at all cost. Expressions of curiosity regarding genital differences and the origin of babies were squelched as unfitting and disturbing anachronisms. Early masturbation was condemned as a sign of ill-boding depravity. The juvenile courts were invoked to crack down on the "delinquent" culprits who

From the Department of Psychiatry, the Johns Hopkins University School of Medicine.

had the temerity to upset the current notions by manual or peeping explorations or playful imitations of adult coitus.

Recent years have brought about a considerable change of these views. Progressive society, liberalized science, humanized medicine and psychology have disposed of the ancient taboo, long enforced by old-maidish compunctions, on anything pertaining to the procreative organs and their functions. Sex is no longer merely a peculiar combination of unmentionable virtue in matrimonial bed chambers, abhorred vice relegated to brothels, and whispered amusement of clubroom wags. Sex literature is no longer mainly pornography peddled and read backstairs. Out of a hazy muddle of obscurity, prudish hoodwinking, emphasis on the grossly abnormal, anecdotal sampling with literary trimmings, circuitous deductions and unpretentious observations comes at the present time the gradual emergence of insight into the sexual development of average children.

Word has come to the pediatricians about infantile sexuality mostly in the form of popularized slogans, which add to the vocabulary but hardly to conceptual perspicuity and familiarity with facts. The pendulum has swung in the opposite direction. Discussion of sex matters, far from being shunned, has become a welcome topic of parlor conversation. The child specialist finds himself confronted by friends, mothers of his patients, social workers, governesses, nursery school teachers and summer camp directors, who seem to be possessed of a knowledge and parade a phraseology in which he does not feel at home. Some physicians respond with puzzled amusement; some are seriously bewildered; some are plainly horrified; some few credulously accept and adopt such wisdom, regardless of its sources. Nearly all feel the need for orientation about a subject which, both because of its wide publicity and its recently gained scientific importance, can no longer be disregarded.

It is the purpose of this review to afford the desired orientation. The topic still abounds and resounds with debate. This is the common and not unwholesome fate of many new issues. Reactions *in statu nascendi* are apt to be more vigorous and engender more heat than at any other time. But out of differences of premises, opinions, and outlooks eventually grows that solidarity which will rest more and more safely on the pillars of demonstrable, objectively obtained and therefore noncontroversial, facts.

HISTORICAL BACKGROUND

The very thought that anything even remotely akin to sexual development and interests could exist before puberty was foreign to writers before the second half of the eighteenth century. There was casual mention, rarely based on reliable information, of miraculously early pregnancies. There were sentimental stories about mature men desperately in love with little girls. There were occasional hints about homosexual relations in imperial Rome between men and small boys. Even in those

infrequent references emphasis was placed on the sentiments and appetites of the adults, the children figuring merely as the objects of love and lust. It is quite possible that, as some have said, the paucity of literary occupation with the subject was based on an attitude of indifference, which took children's sex play for granted and considered it as a common occurrence. Certainly, masturbation must have been observed in early life, yet ancient and medieval writings are singularly free of concern over it.

An almost abrupt change was brought about in France under the influence of Rousseau and Tissot. Rousseau's *Emile* appeared in 1762; in the fourth book of this work, the author ventured to advise parents and educators with regard to the apparently current question of sex instruction. Said he:[44] "Should we enlighten children at an early period as to the objects of their curiosity, or is it better to put them off with decent shams? I think we need do neither. In the first place, this curiosity will not arise unless we give it a chance. We must therefore take care not to give it an opportunity. In the next place, questions one is not obliged to answer do not compel us to deceive those who ask them; it is better to bid the child hold his tongue than to tell him a lie. . . . Lastly, if you decide to answer his questions, let it be with the greatest plainness, without mystery or confusion, without a smile. It is much less dangerous to satisfy a child's curiosity than to stimulate it. . . . Complete ignorance with regard to certain matters is perhaps the best thing for children; but let them learn very early what it is impossible to conceal from them permanently. Either their curiosity must never be aroused, or it must be satisfied before the age when it becomes a source of danger. . . . If you wish to establish law and order among the rising passions, prolong the period of their development, so that they may have time to find their proper place as they arise. Then they are controlled by Nature herself, not by man; your task is merely to leave it in her hands." In other words, let well enough alone and delay the sexual "awakening" as much as possible.

In 1760, almost simultaneously with Rousseau's plea for the preservation of childhood innocence, Tissot,[45] preceded by a few less significant blasts, sounded a shrill warning against the results of masturbation. The worst possible future, the most dangerous and hopeless physical and mental diseases were predicted for the poor offenders. As a result, "sex education" was advocated, which was intended to deter people from ruining their lives and incurring the perils of insanity and locomotor ataxia, which were believed to be the frequent sequels of masturbation. It is well worth knowing that no such apprehensions existed then among the population. Folklore, which seizes readily upon every human activity and ailment, has not deemed the habit sufficiently important to give it any attention. It was reserved for medical alarmists, some of whom were recognized celebrities, to disrupt the serenity of the public by means of

unfounded and harmful scares. The ululations, inaugurated by Tissot, continued unabated for one and a half centuries, relegated mostly to the uninformed laity but cropping out much too often in the attitudes of physicians consulted by perplexed parents. Hufeland[29] came out with a similar tale of horror in 1797. Lallemand,[36] around 1840, added the weight of his authority to the ominous forebodings. As late as in 1902, Rohleder[43] referred to the practice as a "vice" and called it in extra fat print one of the widest-spread popular "diseases": "Yea, I go even further, the widest-spread by far . . . I claim even syphilis and gonorrhea are not so wide-spread as masturbation." He predicted destructive effects on various organs of the body and often on several organs at the same time or successively. He coined for the results of indulgence the horrid term "sexual cerebrasthenia" and distinguished three stages of its progression: the stage of physical and psychic malaise and a change in the physiognomy (the "circles under the eyes" of dubious fame); the stage of internal, especially nervous, diseases; and the stage of mild psychoses. Guided by such mistaken notions, physicians condoned and even recommended corporal punishment, threats of castration and physical restraint as forms of treatment of a habit that was regarded as severely pathological in itself and in its allegedly disastrous consequences.

Griesinger,[25] the noted German psychiatrist, was among the first to adopt a somewhat calmer view about masturbation. In his textbook (1845), he still maintained that "it is an important and frequent cause of insanity, as of all other physical and moral degradation." However, he thought of it as an indirect rather than primary cause because of "that constant struggle against a desire which is ever overpowering, and to which the individual always in the end succumbs—that hidden strife betwixt shame, repentance, good intentions, and irritation, which imperiously impels to the act." He considered children especially jeopardized by the habit because its effect "seems to be greater in proportion to the earliness of the age at which the constitution is injured." In the second half of the past century, authorities began to make a few more concessions. Excessive indulgence only was believed to lead to calamity. Predisposed people only were said to become the victims of the dreaded aftermath. In some quarters, children's masturbation came to be regarded not so much as the cause and precursor of sickness, but in itself a result or manifestation of serious innate psychopathy. But whether it be looked upon as cause or symptom of degeneracy, grave concern persisted everywhere at least until the turn of the century.

Aside from masturbation, there were but few scattered statements in the literature about the sexual development of children. Moll[39] complained as late as in 1909: "When we consider the enormous importance and great frequency of the sexual processes of the child, we are positively astounded at the manner in which this department of knowledge was

ignored by those who have written on the science and art of education, and by those psychologists who have occupied themselves in the study of the mind of the child. Has it been a false notion of morality by which these investigators have been withheld from the elucidation of the sexual life of the child? Or has the reason merely been their defective power of observation? As a matter of fact, I suppose that both these causes have operated in producing this remarkable gap in our knowledge." To be sure, the investigators scanned carefully the autobiographies of famous people (usually the more eccentric among them) and the anamnestic data in the case histories of criminals, prostitutes and psychotic patients for childhood reminiscences of sex behavior. They reported recollections of the sort of persons who would write them unsolicited letters, men and women whose personal problems, coupled with the desire to make their "cases" sound interesting, surely did not allow their experiences to be considered as average. Many, chiefly Krafft-Ebing,[35] recorded instances of gross "perversions" in children; those records concerned themselves more with descriptions, classifications and ancestral backgrounds than the feelings and attitudes of the patients themselves.

Since most of the observations were made and discussed by medical men, it is obvious that ordinary everyday behavior could not and did not come in for consideration. The reports dealt almost exclusively with that which was glaringly disturbing, with extraordinary, exceptional conduct, with children who were the more or less willing objects of assaults by adults. A large portion of the cases, in fact, recruited itself from institutions for the feebleminded, correctional schools, and criminal court procedures. One might assume that occupation with the sex behavior of normal children was a part of the psychologists' domain. But those nineteenth-century psychologists who had anything at all to say about sex were satisfied with the assumption of the existence of something that was variously referred to as sex instinct, sex impulse, voluptuousness, libido or lust; this "instinct," held in abeyance for years, suddenly "woke up" around the time of puberty and began to intrude itself upon the life of the individual. Hence, some of the otherwise excellent books on childhood psychology, such as those by Baldwin[2] (1894), Gaupp[23] (1907) and Groos[26] (1911), omitted even the mere mention of prepuberty sexuality. Dessoir[10] was one of the very few exceptions. He distinguished (in 1894) three stages of the "sexual impulse": the neutral stage, in which the child is not as yet attracted to anyone in such a manner that one would feel justified in assuming the presence of a psychosexual process; the undifferentiated stage, in which the direction of the impulse is diffuse, depending on the external stimulations that happen to be around; and the stage of heterosexual orientation. Dessoir had not derived his conclusions from the study of children but again from the histories of the development of morbid phenomena.

With the advent of the current century came a spurt of interest in children's behavior, prepared by eminent Swiss, German and Italian educators, and psychologists of the caliber of Binet in France and Sully in England. Abstract thought about children was supplemented by direct observations and investigations of children. Average sexual behavior began to be included in the studies. Ellis,[12] compiling a truly inexhaustible range of informative material, made valuable contributions. Moll[29] published in 1909 the first comprehensive monograph on the sexual life of the child. Bell,[3] in 1902, was one of the first to seek knowledge from the study of the activities of everyday children themselves. In 1905 Freud[16] presented a verily fascinating theory of infantile sexuality, which has since enjoyed an ever increasing popularity, influenced contemporary thought and so widely entered into psychiatric, psychologic, educational and belletristic literature, that a discussion of the subject must dwell at some length on its principles and implications.

THE PSYCHOANALYTIC THEORY OF INFANTILE SEXUALITY

"As early as 1896," so Freud once stated, "I had already emphasized the significance of childhood for the origin of certain important phenomena connected with the sexual life, and since then I have not ceased to put into the foreground the importance of the infantile factor for sexuality." He formulated his views comprehensively in 1905 in the second and part of the third of his *Three Contributions to the Theory of Sex*, which are entitled: "The Sexual Aberrations," "Infantile Sexuality," and the "Transformations of Puberty."[16] Some of the opinions then expressed have since then undergone revisions or elaborations, but the essential features are still held valid by the psychoanalytic school.

According to the Freudian theory, the sexual impulse is present from the beginning and shows typical stages of development, which are biologically determined, admit of individual variations, and are subject to cultural influences. The impulse derives its earliest satisfactions from the self. The infant goes through an initial period of pregenital organization, in which the striving for the acquisition of pleasure finds its objects in a number of so-called erogenous zones. An erogenous zone is defined as "a portion of skin or mucous membrane in which the stimuli produce a feeling of pleasure of definite quality," and "the sexual aim of the infantile impulse consists in the production of gratification through the proper excitation of this or that selected erogenous zone." Such a zone "often retains for life a considerable fragment of genital irritability," though in the main the pregenital stage does not extend beyond the third year of life. In the course of its duration, two phases are distinguished. In the oral or cannibalistic phase, of which thumb-sucking is a "model" expression, "the sexual activity is not yet separated from the taking of nourishment," and "the sexual aim consists in the incorporation of the object into one's body"; the mouth is the

erogenous zone, and the acquaintance with its pleasurable stimulation has been furnished by "the first and most important activity in the child's life, the sucking from the mother's breast (or its substitute)." In the anal phase, the anus and excretory organs function as erogenous zones: "Children utilizing the erogenous sensitiveness of the anal zone can be recognized by their holding back of fecal masses until through accumulation there result violent muscular contractions; the passage of these masses through the anus is apt to produce a marked irritation of the mucous membrane.; besides the pain this must produce also a sensation of pleasure." Anal eroticism contains a contrast between activity and passivity, the former being supplied "by the musculature of the body through the mastery impulse," the latter by the erogenous mucous membrane of the bowel, which "manifests itself above all as an organ with a passive sexual aim." The contrasting pair of impulses, the one containing the nucleus of aggressiveness and sadism, the other of submissiveness and masochism, "are developed in almost the same manner." Hence, there is in the human no pure aggression or submission, that is, no pure masculinity and femininity: "On the contrary, every individual person shows a mixture of his own biological sex characteristics with the biological traits of the other sex and a union of activity and passivity."

Between the third and sixth years of life, the sexual strivings converge upon the genital area. In Freud's earlier writings, the primacy of the sexual organs was not supposed to assert itself before puberty; it was moved back to preschool age in 1923,[19] when a phallic stage was "interpolated as a third phase in the development of the child after the two pregenital organizations." At the beginning, the child is still autoerotic or narcissistic: the self is still the object of his libidinous desires. The sexual aim, however, commences to reach out beyond the confines of his own body. There is a "short flourishing period of sexual activity at about the fourth year." Sexual inquisitiveness makes its appearance. In fact, all curiosity ("the impulse for knowledge and investigation") is fed by the energy which comes from the "looking impulse," the desire to see the genitals of the opposite sex. The first such experience evokes in the boy, who has presupposed in all persons a genital like his own, a "severe internal struggle," referred to as castration complex, associated with a stubborn defense "against the contradictions which soon result" and fear of the loss of his own penis. In the girl, the discovery of the genital differences leads to penis envy and the desire to be a boy. The sexual object shifts from the erogenous zones to the outer world. The first choice is that of the parent of the opposite sex, in whom the child invests his libido. A boy wishes to monopolize his mother for a love object and hates his father as a powerful rival. This situation is spoken of as the Oedipus complex, a term derived from the Grecian tragedy in which Oedipus, driven by uncontrollable forces, unknowingly

kills his father and marries his mother. (In girls, the analogous "family drama" is sometimes spoken of as the Electra complex.) Such an attitude gives rise to guilt because of the incestuous nature of the child's love, and fear of the competitor's revenge. Normally, the child comes to renounce this conflict by giving up his real parents and substituting new ideals: "The father ideal furnishes the goal of manliness and masculinity towards which he strives. The mother ideal supplies him with the vision of a love object which he may freely seek; both act as guiding principles which lead him towards maturity." The Oedipus complex is considered as the nucleus of every neurosis. The child is not aware of all or most of these happenings, which take place in the unconscious.

At about five years of age, there comes a time of relative quiescence of the sexual impulse, the so-called latency period, which lasts until the onset of puberty. The child has already some time before begun to repress desires and feelings which are prohibited by convention and interfere with smooth adjustment. Repression is thought of as the elimination from consciousness of such wishes and ideas, which are said to become submerged into the unconscious. They retain great dynamic significance and may break through in the symbolism of dreams, lapses of the tongue and pen, and neurotic symptoms. Freud ascribes the failure to remember early childhood occurrences to the need for repressing the sexual tensions, cravings, and manifestations of that age. During the latency period, "the psychic forces develop which later act as inhibitions on the sexual life and narrow its direction like dams. These psychic forces are loathing, shame, and moral and esthetic ideal demands." Sublimation sets in, a compromise adjustment springing up from conflict, by virtue of which the energy of infantile sexuality is "turned away either wholly or partially from sexual utilization and conducted to other aims." All affectionate impulses "were originally of a completely sexual nature, but have become inhibited in their aim or sublimated. The manner in which the sexual instincts can thus be influenced and diverted enables them to be employed for cultural activities of every kind, to which indeed they bring the most important contributions."[20] Portions of the sexual manifestations which have withdrawn from sublimation may occasionally break through in childhood as well as in later life.

Before a child has achieved the indelible erection of the dams against sexual transgressions, dams of loathing, shame and morality, he is considered to be polymorphously perverse and may be misled into all sorts of seductions. Every step on the road of the development of infantile sexuality may become a point of fixation, an undue amount of libido being anchored to some phase which is ordinarily left behind in further growth; thus an unusually strong libido investment may remain permanently attached to any one preliminary stage, and in later years the not

fully satisfied instinctive desires may return to the points of fixation. Factors influencing the evolution of sex life and personality are summed up as variations in the sexual constitution ("a preponderance of one or another of the manifold sources of sexual excitement"), qualifications and new possibilities "depending upon the fate experienced by the sexual streams originating from the individual sources" (so-called further elaborations), the modes of repression and sublimation, accidental experiences (the "sex trauma," to which Freud has in later years attached less importance than originally), fixations, and the preneurotic existence of "spontaneous sexual prematurity," which causes "a breaking through, shortening or suspending of the infantile latency period." Character "is built up to a great extent from the material of sexual excitations; it is composed of impulses fixed since infancy and won through sublimation, and of such constructions as are destined to suppress effectually those perverse feelings which are recognized as useless. . . . Certain character traits are known to stand in relationship to definite erogenous components. Thus obstinacy, stinginess and orderliness are traceable to anal erotism. Ambition is determined through a marked urethral disposition."

Such is the essential structure of the psychoanalytic theory of infantile sexuality, reproduced almost entirely in the words of Freud himself. The theory was formulated and published four years before Freud or anyone else had ever analyzed a child. When, in 1909, he did record in a 109-page article the "Analysis of a Phobia of a Five-Year-Old Boy,"[18] he believed that his one direct interview with Little Hans fully confirmed his previously established views. A number of Freud's pupils began to occupy themselves with children. At first they illustrated their statements largely with quotations from works of fiction and casual observations made by themselves or reported by others. Later, children were analyzed and methods were devised, which were intended to adapt to children's needs the analytic procedure that had been worked out for adults. Jung[31] (1909, 1910), Hug-Hellmuth[30] (1913), Abraham[1] (1916), Bernfeld[4] (1917), and Deutsch[11] (1919) were among the first to take up, discourse, and enlarge upon Freud's theory of infantile sexuality. Freud's daughter, Anna,[14] and Melanie Klein,[33] using markedly different procedures, have laid down in monographs their experiences and deductions derived from the protracted analyses of a small number of children. Among the pediatricians, Freud has found an enthusiastic supporter in Friedjung.[21] In the past decade, many psychoanalysts have offered additions to the existing case reports and contributed further details and elaborations. The infantile ideas about sex differences and puzzlement about the origin of babies (dubbed by Freud "the Riddle of the Sphinx") were explored more minutely. Freud's various stages of sexual development were given more detailed attention. The oral erotic phase was subdivided into a sucking and biting level,

bearing on the evolution of submissive and aggressive trends. In the whole, however, the Freudian structure has been retained in its basic features.

CRITIQUE OF FREUD'S THEORY OF INFANTILE SEXUALITY

Freud has made two fundamental contributions to the study of infantile sexuality. He has definitely established and emphasized the fact that the sexual potentialities inherent in the species evolve from an early age and, when puberty is reached, much that has preparatory significance for the shaping of sex conduct has gone on for years within and without the individual. Freud has furthermore realized that childhood experiences concerning the type of satisfaction of sexual curiosity, masturbatory habits, and the attitudes of the adults are by no means to be regarded as isolated phenomena, detached from a child's general personality development. He has shown that the puzzlements, curiosities, explorations, informations and misinformations, discoveries, warnings and threats connected with the genitals and with procreation are integrated into the biographic dynamics of growth and character formation. With these pioneering recognitions and teachings, Freud has undoubtedly come to occupy and justly claim first rank among the students of infantile sexuality.

With humility born of profound admiration for the man and his contributions and at the same time with a sense of obligation towards objectivity and the postulates of logical thinking, this reviewer undertakes to subject the psychoanalytic theory to that kind of scrutiny which every scientifically oriented doctrine should be willing and even anxious to submit.

To begin with, the entire theory of infantile sexuality was ready-made before even one child was ever so much as seen professionally by Freud or any other psychoanalyst. Freud had examined adults with his special technique and arrived at his conclusions from his interpretations of their dreams, so-called free associations, and psychopathologic symptoms, the analysis of which brought forth statements accepted as recollections of occurrences and sentiments in early childhood. These reported memories were obtained in a setting in which Freud avowedly "searched directly for the sexual origin of the neuroses." Even if the memories had been correctly reproduced (something for which proof could rarely be furnished), it is necessary to realize that the people who expressed them were psychiatric patients suffering from more or less severe personality disorders. It would be difficult to imagine a scheme explaining the normal development of visual phenomena on the basis of reminiscences of adults affected with eyesight disturbances, or a system of infant nutrition based on the artificially revived memories of adults treated for gastrointestinal diseases. Yet the interpretations of retrospective utterances of abnormal adults, who often could not even see

contemporary events and relationships in their proper perspective, served for the erection of a detailed and all-inclusive doctrine of infantile sexuality.

To be sure, Freud at first expressed himself with admirable caution. In the 24 pages (Modern Library edition) of Brill's reliable translation of the second of the *Three Contributions to the Theory of Sex*,[17] there are not less than 50 qualifications (not counting those in the footnotes), such as "probably," "possibly," "perhaps," "apparently," "it seems," "as it were," "so to say," "I believe," "we can venture the opinion," "it is easy to conjecture," "it may be assumed." Nobody can or should be denied the right to assume and conjecture. But this caution was promptly abandoned, and even in the selfsame chapters the probabilities, possibilities, semblances, impressions, beliefs, and assumptions were given categorically the status, which has been claimed for them to this very day, of undeniable eternal verities.

The assumptions themselves had their origin in various sources, of which the analytically interpreted memories were only one set. Freud has made ample use of analogies, both to build up and to substantiate his suppositions. His analogies were frequently of a nature that would gravely disturb any logician. If two complex situations, each containing a host of dissimilar features, showed one or two resemblances, then the total situations were readily pronounced as being equal in character. Two examples may suffice. Freud stated that thumbsucking "is connected with an entire exhaustion of attention and leads to sleep"; adult sexual intercourse also exhausts and leads to sleep and is, in fact, "the best hypnotic." Hence it was concluded that thumbsucking and adult coitus are closely related phenomena affording sexual gratification. Freud remarked that thigh rubbing is the preferred form of girls' masturbation and that boys make greater use of the hand for this purpose; he took it tacitly for granted that the hand is a symbol of domination. Hence he concluded: "The preference for the hand in boys already indicates what an important part of the male sexual activity will be accomplished in the future by the impulse of mastery." Such divagations are by no means sporadic. It would be unfair to criticize a whole elaborate system by digging up a few digressive lapses. But statements of this type abound and are often used as intrinsic links in the chain of reasoning. The underlying mode of finding analogies is made a definite part of the methodology; it has been brought to a probably unsurpassable climax in the reports of children's analyses by Melanie Klein,[33] whom even some of the psychoanalysts are anxious to disown.

Another sin against logic was committed by the habit of making broad generalizations, of drawing sweeping inferences from arbitrarily selected observations, experiences, and anecdotes. Part features which may or may not be essential to a whole performance were often lifted out of the totality, interpreted on the grounds of pre-established premises and then

made to impart the interpreted meaning to the entire performance. Nursing at the breast, for example, was taken for the first oral erotic gratification. To prove this, Freud asserted: "He who sees a satiated child sink back from the mother's breast, and fall asleep with reddened cheeks and blissful smile, will have to admit that this picture remains as typical of the expression of sexual gratification in later life." There was an even stronger tendency to attribute universal validity to impressions gained from a limited number of observations. This is especially true of the universal application given to what Freud has termed Oedipus complex, castration complex, and penis envy.

Sometimes no proof whatever was offered by Freud for the assumed connections between two separate phenomena. The mere statement of relatedness was deemed sufficient and was indicated by nothing more than a sequence of sentences, leaving it to the reader to regard sequence as coherence. For instance, Freud spoke of sexual excitation by means of "rhythmic mechanical shaking of the body." Such shaking, he said, "seems to be of a pleasurable nature." In the very next sentence, it no longer "seems" so, but "is proved by the fact that children are so fond of play involving passive motion, like swinging or flying in the air, and repeatedly demand its repetition." Then follow two sentences which by their presence alone are to convey the impression of relatedness and to serve as a step in the argument: "As we know, rocking is regularly used in putting restless children to sleep. The shaking sensation experienced in wagons and railroad trains exerts such a fascinating influence on older children, that all boys, at least at one time in their lives, want to become conductors and drivers." Following this, the "exquisite sexual symbolism" of traveling is simply taken for granted.

All such assumptions, analogies, generalizations and juxtapositions culminated in the assignment of all-momentousness to infantile sexuality, which is said to determine, shape, and control all thoughts, feelings, actions, and omissions of the individual during his entire life span. All cognition, conation and emotion, all character traits, all satisfaction and dissatisfaction, all culture, fiction, art and religion, the selection of a mate and the choice of a vocation, all relationships to other people, all symptoms of mental and—as has been claimed more recently—physical illness, everything that a person does or does not do is declared to be predestined by the early development of the sexual impulse, by the manner in which repression, sublimation, and fixation operate in the years of childhood. It is true that Freud and his followers have again and again pleaded that the psychoanalytic concept of libido is not to be restricted to what is called sex in the narrow sense of genital gratification. It is to comprise every kind of pleasure and pain sensations and every kind of attachment and aversion. This plea deserves to be heeded. Freud has a right to define, delimitate or broaden his concepts. Clear explanation of a term one uses must certainly be hailed as a con-

siderable help toward understanding. Unfortunately the psychoanalytic school itself, including Freud, has created a semantic confusion by failing to adhere to its own definition. Nearly all activities of children and adults, even the "impulse for knowledge," are time and again referred to gross sexual behavior in the old and narrow sense. Notwithstanding all pleas and protestations, the psychoanalysts have expended a great deal of effort and suasion to keep the interpretations of human conduct within a limited range of genitally centered possibilities.

It may be that biologic theories are not to be measured too strictly on the basis of logical reasoning. Logic is, after all, a system of man-made formulations. Biologic happenings are not determined by man; if their existence is discovered, it matters not whether they do or do not fit into any system devised by human beings; the main thing is that they happen. All preceding criticism would deservedly collapse as soon as at least some of the major claims can be demonstrated as being rooted in facts. Freud has said gleefully: "I can point with satisfaction to the fact that direct observation has fully confirmed the conclusion drawn from psychoanalysis, and thus furnishes good evidence for the reliability of the latter method of investigation." He referred therewith to his analysis of Little Hans.[18] Five-year-old Hans had developed a fear of being bitten by a horse. His father was a physician designated as one of Freud's "closest adherents"; his mother was an expatient of Freud who had treated her for a "neurosis" of an undisclosed character. Both parents had agreed that "in bringing up their first child they would use no more coercion than might be absolutely necessary for maintaining good behavior." Consistency was not one of their outstanding assets; their "agreement" and enthusiasm for psychoanalysis did not prevent the mother from threatening to cut off the child's penis when she found him touching it at 3½ years of age, or from taking him into her bed. The "treatment" of the phobia was undertaken by the father under Freud's direction. The father told his son that his "anxiety was the result of masturbation, and encouraged him to break himself of the habit." He told his son that by his fear of horses he was trying to replace his affection for his mother. He told his son that "the threat of castration made to him by his mother 15 months earlier was having a deferred effect upon him." He told his son that "he was afraid of his father because he, himself, nourished jealous and hostile wishes against him," and "that the horse must be his father." After four months during which these "interpretations" were decreed upon Hans who was at no time consulted, the father learned that all the while Hans had not only been afraid of horses biting him but also "of carts, furniture vans, busses, of horses that started moving, of horses that looked big and heavy, and of horses that drove quickly." The father, with Freud's help, decided that all these fears had one feature in common: "the fear of horses falling down." Hans was told that, since horses represented his father, he

must have wished that his father "might fall down in the same way and be dead." When Hans began to "show disgust at things that reminded him of evacuating his bowels," this was promptly interpreted as an "analogy between a heavily loaded cart and a body loaded with feces, between the way in which a cart drives out through a gateway and the way in which feces leave the body." Hans was also wishing, by decree, that his mother might drop his little sister, of whom he was jealous, while she was being given her bath, so that she should die. In fact, feces symbolized his sister, because—so Freud and the father thought for Hans—he identified defecation with childbirth: "We can now understand that all the furniture vans, drays and busses were only stork-box carts (symbolic representations of pregnancy); and that when a heavily loaded horse fell down, Hans can have seen in it only one thing—a childbirth, a delivery. . . . Thus the falling horse was not only his dying father, but also his mother in childbirth." When all such interpretations failed to reduce the child's fears, Hans was led into the presence of the Professor. Freud did not waste his time giving Hans a chance to express himself. He "disclosed" to Hans "that he was afraid of his father, precisely because he was so fond of his mother." He told him many other things. Hans was duly impressed by the Professor's instant knowledge of things about him which he himself did not know (even though his father had hammered them into his head for months).

Those were the "facts" which "fully confirmed" Freud's conclusions. A fearful, peculiarly trained little boy was made the passive recipient of wilfully decreed "interpretations" of his fears. He was given the benefit of that "especially energetic assistance" which a child required "on account of small development of its intellectual system." Proof was indeed not necessary. Objectivity was an unneeded encumbrance: "For a psychoanalysis is not an impartial scientific investigation, but a therapeutic measure. Its essence is not to prove anything but merely to alter something." *Sic volo, sic jubeo!* The same pattern was followed in later analyses as well. This type of interpretations has achieved veritable orgies in the child analyses of Melanie Klein. Intended to explain the dynamics of children's behavior, it portrays the dynamics of the behavior of uncritically self-assured theorists, bound to neither logic nor facts.

These dynamics cannot be fully understood without the knowledge of the broader premises underlying Freud's theory of infantile sexuality. The concepts of libido, erogenous zones, Oedipus and castration complexes, latency period, repression, sublimation and fixation depend on the presupposed existence of an unconscious. The unconscious, which is according to Freud "the appropriate and justified expression for an established fact,"[17] is that part of the "psyche" which is not accessible to awareness and is invested with energy, forces and drives. Consciousness is but "a sense organ for the perception of psychic qualities." Between it and the unconscious stands the preconscious, through which

repressed material, lodged in the unconscious, can reach awareness after it has been blue-penciled, disguised, and distorted by a special kind of censorship. The unconscious itself is subdivided into three parts. The ego represents the personality as it communes with the outside world. The superego, a modified part of the ego, is "the representative of our parents; when we were little children, we knew these higher natures, we admired them and feared them, and later we took them into ourselves." The id represents the instinctive drives, the sole aim of which is the gratification of all needs. The unconscious, thus constituted, is "the true psychic reality, a special form of existence which must not be confounded with material reality." The psychoanalytic method, by means of deductions and interpretations of which we have given a few examples, holds alone the key which can unlock the otherwise tightly closed door to this psychic reality.

Some critics might point to the ease with which abstractions are being constantly personified. This method is very much in evidence when a tripartite psyche, harboring a tripartite unconscious, is made the tumbling ground of forces, impulses, mechanisms, complexes, censorship, etc. Moreover, all these and other abstractions (a death instinct was later given prominence as a counterpart of the libido instinct) have their goals, act and interact, intermingle and separate, transform, disguise, displace, repress, sublimate, fixate, are kept in abeyance or break through, and in funnel fashion always converge on infantile sexuality. Such criticism is quickly and impatiently met with the assertion that the "reality" is not to be thought of as real and the "established fact" is not to be looked upon as factual. The existence of the unconscious, Freud's "greatest discovery," must be fully accepted. Yet this existence is declared to be not really existent but a "working hypothesis," similar to the newer hypotheses in physics. However, despite this seeming concession to logic, the same inconsistency and unconcern which unhesitatingly turn assumptions into actualities continue to anthropomorphize all these abstractions freely and abundantly. Discursive repetitions act as self-convincing evidences and are fully expected to convince others.

In recent years, revolt has arisen in the ranks of the psychoanalysts themselves. No one, it is true, has ventured to apply the ax to the basic premises. But many have washed their hands of the "absurdities" perpetrated by some of the more unbridled speculators and interpreters. Karen Horney[28] has had the admirable courage to examine the Freudian concepts without the usual apostolic zeal and aggressive defensiveness of Freud's adherents. She has recognized many of the inconsistencies and said so with tactful frankness. She has taken especially vigorous issue with Freud's doctrine of "repetition compulsion," according to which adult psychic life is regulated by "the tendency of instincts to repeat experiences or reactions already established" in childhood. She has pointed out the relative sterility of an attitude which knowingly

neglects all factors other than sexual and all experiences other than infantile. She has cleverly tried to sweep some of the most glaring fallacies out of the psychoanalytic structure.

OBSERVATIONS MADE ON CHILDREN

In 1902, three years before Freud's presentation of his theory, Bell[3] published a paper which has since then been often mentioned but rarely read. Bell was at the time affiliated with Clark University at Worcester, Mass., where seven years later Freud, at Stanley Hall's invitation, made his personal appearance before an American public and Jung, one of his earliest disciples, gave a lecture on "conflicts in the psychic life of the child." Bell's paper was based on reports of actual observations made by himself and 360 teachers in coeducational public schools. His material extended over 2,500 children "who were under the ordinary social and industrial conditions." On the basis of these experiences, Bell divided the infantile manifestations of "the emotion of love between the sexes" into two stages.

The first stage, lasting from three to eight years of age, was said to be characterized by the following evidences of the emotion: "Hugging, kissing, lifting each other, scuffling, sitting close to each other; confessions to each other and to others, talking about each other when apart; seeking each other and excluding others, grief at being separated; giving of gifts, extending courtesies to each other that are withheld from others, making sacrifices such as giving up desired things or foregoing pleasures; jealousies, etc." Though Bell spoke of these actions as referable to sex origin, he did not want them at this early age to be looked upon as specifically sexual, except in some children whom he considered to be precocious. He described the manifestations in preschool children as spontaneous, profuse and unrestained: "There is an absence of shyness, of any sense of shame, of the feeling of self-consciousness. The children have as yet no notion of the meaning of sex. Their naïveté in this regard has not been destroyed by the social suggestion that such actions are wrong and vulgar."

The second stage, extending from the eighth year of life to about the twelfth year in boys and the fourteenth in girls, was said to be characterized "by the appearance of shyness, of modesty, especially in girls, of self-consciousness and consequent efforts toward self-repression; by the inhibition of the spontaneous, impulsive love demonstrations so freely indulged in during the previous stage. . . . There is a conspicuous absence of pairing. The lover and sweetheart are not often seen alone together. . . . Gifts are nearly always delivered in some secret manner, in many instances of which the giver leaves no clue that would reveal his identity. . . . Another indication that will not escape the close observer is that of the boy lover off at a distance, feasting his eyes upon

every movement of his girl who may know absolutely nothing about his devotion. . . . However, the emotion has its expression indirectly through games, plays, and other incidents that can be used as masks. Instead of direct contact of personalities through the love confession as such, it is long-circuited through some conventionality. In this regard the games of children are used very effectively. . . . In this, as in the previous stage, the embrace is the most important love expression and stimulus. But in this stage it takes on disguised forms or is excused by the ceremony of the games. . . . The kiss is not the frank love kiss given and received as such, but one called for by the rules of the game. This makes the kissing relatively impersonal and enables the young lovers thoroughly to enjoy the love communication without the awkward embarrassment that would come to them if the expression were not thus long-circuited through the game." Besides games, there are other means of manifesting the "emotion," such as eye glances, managing some way of sitting together at school, showing off, and teasing. Until nine years of age, girls are more aggressive than boys in love affairs. "At this age the girl's modesty, coyness, and native love for being wooed, come to the surface, and thereafter characterize her attitude toward the opposite sex."

The chief merit of Bell's communication, which was illustrated with a representative number of "typical cases," consisted in the fact that here for the first time an effort was made to record the observed amorous behavior of average children. Erections, masturbation, evidences of sexual curiosity, and attractions to children of the same sex were not within the scope of Bell's studies. Bell did not prove the sexual basis for some of the actions brought together under the heading of "the emotion of love." Some of his inferences are open to discussion. But he has shown a direction which promised to yield valuable information. This direction, however, was not followed in this country for a long time.

In Germany Kötscher[34] published in 1907 a booklet which proposed to deal with "the awakening of sex awareness and its anomalies"; in it he dwelt almost entirely on adult sex behavior, referring to children only occasionally and rather vaguely. In 1909 Moll's book, *The Sexual Life of the Child*,[39] summed up all that was then known about the subject, at the same time adding important original contributions. Overshadowed for years by an avalanche of psychoanalytic literature, it has long been put aside as an "old-fashioned and obsolete" bibliographic item. Freud has expressed himself about it in a derogatory manner. Moll offered factual material and generally refrained from hasty conclusions. His open-mindedness did not always prevent him from indulging in unwarranted alarmist diagnoses of morbidity.

Moll divided childhood into two periods, before and after the end of the seventh year. He divided sexual behavior into two distinct phases:

contrectation and detumescence. Contrectation was defined as a "process tending toward bodily and mental approximation to another individual." Detumescence described "the sex impulse in so far as it is confined to the peripheral organs," namely the genitals. In normal adults, "the two components are so intimately associated that they can as a rule be separated only by artificial analysis." As for children, according to Moll, "the occurrence of manifestations of the sexual impulse during the first period of childhood must arouse suspicions of the existence of a congenital morbid disposition," except for the "phenomena of detumescence," if they do not appear spontaneously but result from either local inflammatory changes or deliberate seduction to the performance of sexual manipulations. Spontaneous detumescence also "aroused suspicion" in Moll when it occurs in the first part of the second period of childhood, before twelve years of age, whereas contrectation after the eighth year did not "justify the inference that any morbid predisposition exists." Thus practically all sexual behavior during the first decade, including that reported by Bell, would have to be considered or suspected as pathologic. This view is not tenable in the light of later insights gained from the study of normal children.

For about twenty years after the first edition of Moll's book, the nonpsychoanalytic study of infantile sexuality was at an almost complete standstill. No one seemed to dare to break through the monopoly created by the Freudian theory. The speculative deluge seemed to have drowned out all curiosity for objective facts. Interpretations took the place of observations. Bell and Moll became dimly remembered episodes. Sometimes questionnaires, such as those of Peck and Wells,[41] Exner,[13] and Davis,[9] sent to college students and college graduates, tried to obtain early data about masturbation. But in the whole, the question of sexual development in normal children during the first decade of life was ignored, except that Malinowski[37] and Margaret Mead[38] made interesting contributions to the knowledge of the sex behavior of children in primitive cultures.

In 1932 Katherine Hattendorf[27] published her collection of a considerable number (1763) of children's questions concerning sex. Those asking them (of their parents) ranged between 2 and 14 years of age. The questions could be classified into 8 groups: Origin of babies (40.9 per cent); coming of another baby (14.5 per cent); physical sex differences (12.7 per cent); organs and functions of the body (11.9 per cent); process of birth (10.4 per cent); relation of the father to reproduction (5.2 per cent); intrauterine growth (2.4 per cent); marriage (2.0 per cent). Preschool children asked 49.1 per cent of the questions, those from 6 to 10 years asked 40.1 per cent, and those above 10 years of age asked 10.8 per cent of all the questions. Miss Hattendorf concluded: "The relatively large number of questions for children of preschool age,

as compared with other ages, indicates that children are manifesting interest in sex through their questions in these very early years. The subject matter of the questions indicates what children are wanting to know in reference to sex. Interest is shown to develop from simple inquiries concerning the origin of babies, through the more intricate physiological processes of conception and birth, to the deeper sociological and psychological interpretations of customs and attitudes. The ages at which the questions occur substantiate the feeling expressed by so many writers that sex instruction should be given in the early years. The questions, in showing the trend of children's interest in sex, seem to indicate a developing interest in the subject which points to the need of a graded program in sex education for children."

CHILDREN'S OWN CONTRIBUTIONS

With the single exception of Miss Hattendorf's inquiries, children themselves had not been consulted as to their own awareness of matters sexual and their own attitudes toward them. Casual actions and utterances were observed, recorded, expounded, suspected or not suspected of morbidity, declared to be common, exceptional, precocious, preneurotic, neurotic, or psychopathic. After all, children could hardly be expected to make direct contributions when consciousness was viewed as a sense organ of the censured, markedly obliterated perception of psychic qualities hidden deeply in the unconscious. Since the "manifest contents" of children's own expressions were believed to be understood only through their interpretations, the expressions themselves were considered inessential and negligible and were utterly distrusted. Besides, there was a justified feeling that when children have reached an age at which they are capable of communicating their opinions, they have already been exposed to influences that make them wary and suspicious of questioning adults, so that their responses do not represent their real attitudes. As a result, they were left alone, and adult thinking and experience were foisted upon them.

It was reserved to Conn[6] to break this impasse. Conn, supported by a grant from Child Neurology Research (Friedsam Foundation), began early in 1937 the study of 200 children (128 boys and 72 girls), ranging in age between 4 and 12 years, at the Children's Psychiatric Service (directed by this reviewer), which is connected with the Henry Phipps Psychiatric Clinic and the Harriet Lane Home for Invalid Children of the Johns Hopkins Hospital. Previous experiences with fearful and carsick children[6] had shown him that personal problems were discussed much more freely in play situations. While direct questions were likely to arouse self-consciousness, evasiveness, or embarrassment, children were able to reveal their attitudes, hopes, fears, ambitions, jealousies, resentments, attachments, etc., with far greater ease by reenacting them in play

through the medium of dolls. The play interview offered them an opportunity for self-expression; they could (and did) speak of their intimate personal affairs "as if" they were those of the dolls and learned to apply to themselves the things which they had transmitted to the dolls. Conn used this method in his investigations of children's sex awareness and sex attitudes. The details of the procedure were not prearranged in the form of a rigid "technique" but allowed to evolve out of the contacts with many children and their responses; their behavior contributed a considerable share to the form which the method gradually assumed. The children's leads were followed as they were given. There was no urging, no grilling, no crude suggestion of any kind. The children had full freedom of speech and motion. The average intelligence quotient was 95.2 per cent. Markedly retarded, acutely ill children, or those suffering from disturbing chronic ailments were excluded from the study. Every child had a physical, psychiatric, and social service examination, guaranteeing a familiarity with the essential facts concerning the child, his biography, personality, general behavior, specific experiences, habits, assets and liabilities, attitudes toward home, school and play life, the family background, and the social and economic situation. The children's own productions were supplemented by their parents' reports about the development of modesty reactions, evidences of curiosity, names given to genitals and toilet functions, any kind of sex play, and attitudes communicated to them by the family, playmates and others. School teachers' reports were sometimes of additional help. All questions and answers were recorded verbatim. Entries were made about any remarkable physiognomic, gestural and postural concomitants, hesitations, criticism of the procedure and parenthetic utterances. Thus each protocol not only represented a detailed replica of everything that transpired during the investigation but also a full life and social history of the child.

It was thus possible to study at the source the development of children's awareness of sex differences, ideas about the origin of babies, feelings of shame, notions about love, courtship and marriage, sexual inquisitiveness, genital manipulations, spontaneous erections, sexual explorations, attractions to the opposite sex, the parents' attitudes and their offspring's reactions to these attitudes. Some of these items have been sufficiently investigated to allow a preliminary summary. Knowledge of the differences in the configuration of the genitals was expressed by 50 per cent of the children between 4 and 6 years of age, 72 per cent each of the 7-to-8 and 9-to-10 year groups, and 86 per cent of those between 11 and 12 years old. In the two middle age groups, the figures for indicated awareness and reported experience of seeing the opposite sex genitals were nearly identical; in the youngest group, 17 per cent more children were known to have witnessed the difference than seemed able or willing to speak about it; in the oldest group, 13

per cent more gave evidence of their knowledge than were ready to report the source of this knowledge. As many as 150 children included differences of attire in their surveys of inequalities between males and females, 116 named genital dissimilarities, 93 referred to tonsorial distinctions, 44 pointed to differences in urination posture, and 9 made reference to the breasts and nipples. Many children recalled the time when they first became acquainted with the shape of the opposite sex genital. Most of them accepted the discovered difference calmly as natural phenomena existing in their own rights. Some reacted with surprise and the feeling that "something was wrong," that reality had somehow not come up to their expectation of sameness. A small number of children assumed temporarily that the female genital had once been like the male and had been cut off, broken off, or lost.

At no time did the children show greater embarrassment than when they were confronted with the problem of naming. "It is not," said Conn, "the thing itself which is dirty, sinful, or gives rise to the feeling of shame, but its verbal symbol. The average child of 5 or 6 who has an opportunity to observe genital differences can say that 'girls have short ones and boys have long ones,' or that 'a boy's sticks out and a girl's doesn't.' This is as much a fact as any other fact which the child has experienced, and he can report what he has seen without any feeling of embarrassment. It is the name or label that he finds great reluctance in divulging. This name may be as innocuous as the terms dew drop, teddy bear, dicky bird, train, or piece of string. Nevertheless, the child becomes restless, bites his lips or hangs his head, and refuses to speak when he is requested to utter the *word* which refers to that particular part of the body." Even so, the 200 children offered not less than 61 names for the genital organs, terms either used commonly or invented for the purpose by an individual child or family group. It could be shown that the reluctance had been inculcated by adults. So was also the attitude of modesty or shame with regard to seeing someone or being seen in the nude; this reaction could in most instances be traced to specific instructions or warnings.

Spontaneous erections were reported to have occurred in preschool age in 38 of the 128 boys, in 18 during the first 2 years of life, usually associated with matutinal fullness of the bladder. Boys and girls of all ages expressed in the play interviews the hedonic sensations produced by genital manipulations with very similar, sometimes identical remarks, such as: "It feels good"; "it makes me feel good"; "I like it"; "it tickles." Sexual fantasies accompanying masturbation (imagined sight or touch of genitals, buttocks or breasts; thought of coitus) were reported by a very small number of boys below 9 years and girls of all ages; most boys of 9 years and above thought of intercourse in connection with the act. The children's attitudes toward the practice indicated various kinds and degrees of conflict between desire and a

feeling of wrongdoing or fear of dire consequences. Remorse and apprehension, however, were not so deep-rooted as they are often found to be in adolescents. The parents' reactions to their offspring's masturbation consisted variously of calm disapproval (in very few instances), distraction of attention from the performance to play or some other activity, indignant reference to "badness" or "disgrace," scolding, bribing, warning of disastrous effects on physical and mental health, punishment (corporal or by denial of privileges), mechanical restraint, castration threats, "painting" the genitals (not uncommon), or resort to circumcision. An attitude of alarm, coupled with disgust, was found to be still widespread among parents, school teachers and many physicians.

Many other items of Conn's rich material are in the process of, or awaiting, analysis. The study, when completed, promises to furnish ample data about the development of "infantile sexuality," about what children know, think, feel and do, about gradual differentiations and the ages and settings in which they occur. The chief merit of Conn's work lies in the fact that it does not propose to "detect" the vagaries of a hypothetic "sex impulse" but endeavors to accumulate prima facie concrete evidence from the behavior, attitudes and utterances (brought out more easily by means of the play method) of a representative number of average children and their parents, with full consideration of actual observations, experiences, family and neighborhood influences, health, intelligence, and relation to the total personality and environmental constellation. Conn has allowed and enabled children to speak for themselves, instead of letting adult theories and interpretations speak for and about them.

SUMMARY AND CONCLUSION

The evolution of our knowledge of childhood sexuality has been reviewed from its beginnings to the present. The whole subject did not become an issue until about the middle of the eighteenth century. People came to view with alarm the realization that children were curious about biologic sex differences and procreation and some were masturbating. Rousseau popularized the problem of sex education, advising that "Nature" be not interfered with and "innocence" be preserved as long as possible. Tissot threw into the public a scare, not as yet overcome, concerning the allegedly destructive results of masturbation. About a century later, instances of gross sexual misconduct of children and childhood recollections of geniuses, psychotic patients, criminals, and prostitutes began to be collected. "Sexology" became a special topic of investigation, based largely on the speculative occupation with a hypothetic "sex impulse," which was at first assumed to "awaken" at the time of puberty. At the turn of the past century, Freud's theory of

infantile sexuality projected this sexual impulse upon the first decade of life. It was built on a metapsychologic foundation of personified abstractions and derived from a mixture of assumptions proclaimed as realities, analogies defying the postulates of logic, sweeping generalizations, discursive juxtapositions, and interpretations of mostly unverified adult memories obtained in a specific manner from psychiatric patients. However, Freud did succeed in removing the prudishness that had barred the way to a dispassionate study of the subject; he demonstrated the fact that the sexual, as all other, potentialities of man develop from the beginning of life and that these developments are integrated into the personality and character formation of each individual. Bell and Moll recorded actual observations made on children, pertaining mostly to behavior in a group. More recently, Hattendorf studied the questions concerning sex asked by children of their parents. Conn has inaugurated a method of getting at children's sex awareness and attitudes regarding matters commonly considered under the heading of sexuality. Thus the study of infantile sexuality has gone through the successive stages of unconcern, alarm, theory, observation, second-hand inquiry, and direct consultation. It has shifted from a stage of being considered as a detached phenomenon to one of figuring as an integral part of the lives of all children.

How does all this concern the pediatrician? The medical child specialist is the natural adviser of parents regarding their children's health and behavior. He is often confronted by people who are puzzled by the question of whether and how sex instruction is to be imparted to their offspring. He is consulted by parents who want to know what stand and actions they should take about their children's masturbation. His opinion is requested about mechanisms, complexes, repression and the whole gamut of psychoanalytic lore which intellectual mothers absorb from popular books and magazine articles, would-be scientific lectures, and conversations over the bridge table. These questions can no longer be met with indifference, evasion, or emotionalism. Parents expect informed counsel.

Sex instruction is being advocated by progressive physicians, psychologists, and teachers as a part of modern child education. The capacity for curiosity is one of the main characteristics of good intelligence. Once it has been aroused, it is bent upon satisfaction and does not suffer itself to be squelched by impatient subterfuges. Repudiated curiosity, which children cannot cast off at will, is forced into illegitimate, secretive quests for gratification. Information is then likely to come from improper sources. Ocular and manual explorations may take the place of verbal explanation. The whole question, rebuffed as indecent by the elders, may assume in the child's mind a magnitude that may lead to preoccupations and perplexities unhealthy because of their secretiveness. But the mere acknowledgment of the necessity for sex enlighten-

ment is not enough. Good intentions alone, unacquainted with real issues, have tended to develop slipshod methods, confusing rather than helping children, and to go to the extreme of blurting out everything regardless of a child's preparedness and degree of comprehension. Teachers have learned to dose education in reading and arithmetic according to grades commensurate with age. The same principle holds true for sex instruction. The investigations reviewed above have contributed much toward the knowledge of children's sex curiosity, awareness, attitudes and grasp in the successive years of childhood. Familiarity with the facts, willingness, the overcoming of harmful prudishness, truthfulness, a dosage adapted to the individual child's developmental and intellectual preparedness as evidenced by the type of questions asked by him, and good common sense are the best requirements for efficient and sensible sex education. Sex curiosity should be met as and when it arises; it is a natural thing and does not have to be injected artificially.

Physicians can do much good or much harm in guiding masturbating children and their parents. There is no excuse nowadays for scares, threats, punishments, and mechanical restraint. Pediatricians have, in fact, an excellent opportunity to do constructive mental hygiene by doing away with such erroneous beliefs and barbarous practices, which have made life miserable for many children. Consternation about impending ruin and insanity as inevitable results should be radically eliminated. Much worry and self-consciousness, many deep-rooted personality difficulties can thus be prevented or at least attenuated. Removal of any local irritation in the region of the genitals, calm prescription of healthy routine and recreation, introduction into the home of physical hygiene, good sleeping arrangements and wholesome interpersonal relations constitute the best and at the same time most effective therapeutic arrangements.[32]

Pediatricians have until recently paid little attention to the whole issue of infantile sexuality and taken even less investigative interest in it. It is therefore the more remarkable that at least one pediatric group, the German Pediatric Association, had at its annual meeting in 1931 a symposium on the sexual development of children, with Gött,[24] Friedjung,[22] and Boenheim[5] as the chief participants. Thus a precedent has been established which, it is hoped, has inaugurated an era of active pediatric interest in the problems of childhood sexuality.

REFERENCES

1. Abraham, K.: Untersuchungen ueber die frueheste praegenitale Entwicklungsstufe der Libido. Internat. Ztschr. f. Psychoanal. 4: 71, 1916.
2. Baldwin, J. M.: Mental Development of the Child and the Race, New York, 1894, The Macmillan Company.
3. Bell, S.: A Preliminary Study of the Emotion of Love Between the Sexes, Am. J. Psychol. 13: 325, 1902.
4. Bernfeld, S.: Die Psychoanalyse in der Jugendbewegung, Imago 3: 283, 1917.

5. Boenheim, C.: Onanie und Nervensystem beim Kinde, Monatschr. f. Kinderh. **51**: 359, 1932.
6. Conn, J. H.: Sex Attitudes and Sex Awareness in Young Children, Child Study **16**: 86, 1939.
7. Conn, J. H.: The Child Reveals Himself Through Play, Mental Hyg. **23**: 49, 1939.
8. Conn, J. H.: A Psychiatric Study of Carsickness in Children, Am. J. Orthopsychiat. **8**: 130, 1938.
9. Davis, K. B.: Factors in the Sex Life of Twenty-Two Hundred Women, New York, 1929, Harper & Brothers.
10. Dessoir, M.: Zur Psychologie der Vita sexualis, Allg. Ztschr. f. Psychiat. **50**: 941, 1894.
11. Deutsch, H.: Der erste Liebeskummer eines zweijaehrigen Knaben, Internat. Ztschr. f. Psychoanal. **5**: 111, 1919.
12. Ellis, H.: Studies in the Psychology of Sex, New York, 1936, Random House. (First published in 1897, 4 volumes.)
13. Exner, M. J.: Problems and Principles of Sex Education: A Study of 948 College Men, New York, 1915, Association Press.
14. Freud, A.: Einfuehring in die Technik der Kinderanalyse, Leipzig, 1925, Internat. Psychoanalyt. Verl.
15. Freud, A.: Psychoanalysis of the Child: In Handbook of Child Psychology, ed. by C. Murchison, Worcester, Mass., 1931, pp. 555-567, Clark Univ. Press.
16. Freud, S.: Drei Abhandlungen zur Sexualtheorie, ed. 2, 1910; ed. 3, 1922, Leipzig, 1905, Fr. Deuticke. (Engl. transl. by A. A. Brill: Three Contributions to the Theory of Sex, New York, 1930, Nerv. and Ment. Dis. Monogr. Ser. No. 7.)
17. Freud, S.: The Basic Writings, transl. by A. A. Brill. New York, 1938, The Modern Library.
18. Freud, S.: Analyse der Phobie eines 5-jaehrigen Knaben, 109 pages, Leipzig, 1909, Fr. Deuticke. (Engl. transl.: Analysis of a Phobia in a Five-Year-Old Boy. In Freud's Collected Papers, Vol. 3. pp. 149-289, London, 1925, Hogarth Press.)
19. Freud, S.: Die infantile Genitalorganisation, Internat. Ztschr. f. Psychoanal. **9**: 168, 1923.
20. Freud, S.: Autobiography, transl. by J. Strachey. New York, 1935, W. W. Norton & Company, Inc.
21. Friedjung, J. K.: Die kindliche Sexualitaet, Berlin, 1923, Julius Springer.
22. Friedjung, J. K.: Die Physiologie und Pathologie der kindlichen Sexualitaet, Monatschr. f. Kinderh. **51**: 343, 1932.
23. Gaupp, R.: Psychologie des Kindes, Leipzig, 1907, Teubner.
24. Gött, T.: Physiologie und Pathologie der kindlichen Sexualitaet, Monatschr. f. Kinderh. **51**: 321, 1932.
25. Griesinger, W.: Pathologie und Therapie der psychischen Krankheiten, Stuttgart, 1845, Krabbe. (Quoted from the transl. by Robertson and Rutherford: Mental Pathology and Therapeutics, New York, 1882, p. 122, Wm. Wood & Co.)
26. Groos, K.: Das Seelenleben des Kindes, Berlin, 1911, Reuther und Reichard.
27. Hattendorf, K. W.: A Study of the Questions of Young Children Concerning Sex, J. Social Psychol. **3**: 37, 1932.
28. Horney, K.: New Ways in Psychoanalysis, New York, 1939, W. W. Norton & Company, Inc.
29. Hufeland, C. W.: Die Kunst, das menschliche Leben zu verlaengern, Jena, 1797.
30. Hug-Hellmuth, H.: Aus dem Seelenleben des Kindes, Leipzig, 1913, Fr. Deuticke.
31. Jung, C. G.: Ueber Konflikte der kindlichen Seele, Jahrb. f. Psychoan. u. psychopathol. Forsch. **2**: 33, 1910.
32. Kanner, L.: Child Psychiatry, Springfield, Ill., 1935 (ser. ed. 1937), Charles C. Thomas, pp. 73-81: 397-413.
33. Klein, M.: Psychoanalysis of Children, London, 1932 (ser. ed. 1937), Hogarth Press.
34. Koetscher, L. M.: Das Erwachen des Geschlechtsbewusstseins und seine Anomalien, Wiesbaden, 1907, J. F. Bergmann.
35. Krafft-Ebing, R. V.: Psychopathia sexualis, New York, 1922, Medical Art Agency.
36. Lallemand, C. F.: Des pertes seminales involontaires, Paris, 1836-1842, Bechet.
37. Malinowski, B.: The Sexual Life of Savages in North-Western Melanesia, London, 1929, George Routledge & Sons, Ltd.
38. Mead, M.: Coming of Age in Samoa, New York, 1928, Wm. Morrow & Co.

39. Moll, A.: Das Sexualleben des Kindes, Berlin, 1909, Walther. (Engl. transl. by E. Paul: The Sexual Life of the Child, New York, 1912, The Macmillan Company. Reprinted 1929.)
40. Peck, M. W.: The Meaning of Psychoanalysis, New York, 1931, Alfred A. Knopf, Inc.
41. Peck, M. W., and Wells, F. L.: On the Psychosexuality of College Graduate Men, Ment. Hyg. **7**: 697, 1923; **9**: 502, 1925.
42. Pfister, O.: Love in Children and Its Aberrations, New York, 1924, Dodd, Mead and Company, Inc.
43. Rohleder, H.: Die Masturbation (ed. 2, 1902), Berlin, 1899, H. Kornfeld.
44. Rousseau, J. J.: Emile, Transl. by B. Foxley, London, 1933, pp. 177 ff., J. M. Dent & Sons.
45. Tissot, S. A.: De l'onanisme or Dissertation physique sur les maladies produites par la masturbation, Lausanne, 1760, A. Chapuis.
46. Ziehen, T.: Das Seelenleben der Jugendlichen, Langensalza, 1931, Beyer.

News and Notes

The meeting of **Region II of the American Academy of Pediatrics** will be held Friday and Saturday, March 22 and 23, 1940, at the Edgewater Gulf Hotel, Edgewater Park, Miss.

The meeting of **Region IV of the American Academy of Pediatrics** will be held at Seattle, Washington, May 31 and June 1, 1940.

The **American Board of Pediatrics** will hold an examination in Seattle on June 2, 1940, following the meeting of Region IV.

Dr. Horton Casparis of Nashville has been appointed a member of the council of the Southern Medical Association from Tennessee, to fill the unexpired term of Dr. Oliver Hill of Knoxville, whose death was recently reported in the JOURNAL.

Dr. John C. Baldwin, Baltimore, Md., died July 3, 1939, of acute coronary occlusion.

Dr. Helmina Jeidell, Denver, Colo., died Aug. 24, 1939. Dr. Jeidell practiced in Salt Lake City for a number of years.

Information Requested: An appeal has been made to the Academy of Pediatrics for information as to placing a patient with a rather peculiar problem. If any member knows of any institution that might accept this patient, will he communicate with the Secretary?

An 11-year-old boy, legs paralyzed from spina bifida, no control of bowels or bladder, unable to walk, above par mentally, probably capable of being educated if this can be made available to him. He has been seen by numerous surgeons, case not operable. There are certain institutions which would take the boy if the family were destitute, which is not the case, and there are others which are beyond the means of the family. He does not need hospitalization, but an institution where he can be cared for and trained.

Dr. Albert B. Sabin, formerly associate of the Rockefeller Institute for Medical Research, has taken up his new duties as associate professor of pediatrics at the University of Cincinnati and Fellow of the Children's Hospital Research Foundation. Doctor Sabin will continue his studies on viruses and the filtrable microorganisms of the pleuropneumonia group. Doctor Sabin will have several assistants, among them Dr. Joel Warren, formerly in the Department of Bacteriology of Columbia University, who will be a Research Associate in the Children's Hospital Research Foundation. Doctor Sabin will receive the Theobald Smith Award of the American Association for the Advancement of Science at its annual winter meeting.

Book Reviews

The Clinical and Experimental Use of Sulfanilamide, Sulfapyridine and Allied Compounds. PERRIN H. LONG, M.D., AND ELEANOR A. BLISS; Sc.D. New York, 1939, The Macmillan Company, pp. 319. Price $3.50.

The seven chapters deal with the historical aspects of sulfanilamide therapy, the chemotherapy of experimental bacterial infections, experimental toxicity and comparative pharmacology of sulfanilamide and allied compounds, the mode of action of sulfanilamide and its derivatives, the clinical use of sulfanilamide, the clinical use of sulfapyridine, of sulfanilyl sulfanilamides and benzylsulfanilamide, the clinical use of prontosil and neoprontosil, and the clinical toxic manifestations of sulfanilamide and its derivatives. The first chapter, dealing with the historical aspects of sulfanilamide therapy, will probably prove to be both the most interesting and useful of the seven chapters. The clinician will be disappointed in finding little that is new concerning sulfanilamide and much that is lacking concerning sulfapyridine, and will frequently be irritated by the caustic criticism of the viewpoints of other workers in the field and by the many dogmatic statements of the authors.

A History of Women in Medicine. BY KATE CAMPBELL HURD-MEAD, M.D., Haddon, Connecticut, 1938, The Haddon Press.

A work as long as this volume, 532 pages, lends itself poorly to a short review. The author assigned herself no small task when she attempted to cover the space between the beginning of time and A.D. 1800. Meticulously, painstakingly, conscientiously has the author covered the years, reviewing the history and customs of the times and interweaving with the general medical trends of each century the part played by women. In portraying those stretches of time of which little written record remains Dr. Mead may be pardoned if her sympathies direct her imagination. But from the time authentic accounts can be obtained the strictest accuracy prevails. She has a passion for detail and the arrangement of facts. Though I have looked up no reference, I know from the way they are presented that none will be false.

If the reader wishes a reference book, this volume will meet all requirements. If, however, the reader reads for enjoyment, I suggest skimming the first quarter, spending some time on Trotula and her work, and again skimming to the last third. The 16th, 17th, and 18th centuries contained a wealth of medical material to which Dr. Mead has given life. Women, of course, are her chief concern but she has portrayed them not as an isolated group, but against the background of the medical practices of their times.

Illustrations are numerous, ancient friezes, photographs of pottery and instruments, old woodcuts, and anatomical diagrams. A clear and interesting picture of the growth of medicine can be obtained from the illustrations alone.

Dr. Mead's style is easy, charming, and varied. Though at times the material is of the nature of bibliography, she presents it in a way to render it more alive, less dry.

The present volume represents half of Dr. Mead's work. Her humor and charming style should make the second volume, 19th century to date, of even greater interest.

K. B.

Nutrition and Physical Degeneration. WESTON A. PRICE, D.D.S. New York, 1939, Paul B. Hoeber, 431 pages. Price, $5.

This is an interesting, important, and thought-provoking book. It is the theory of Dr. Price that something is either essentially lacking or present in the diet of primitive peoples as contrasted with that of the civilized white, which prevents dental caries and abnormalities in facial and dental arch formation. In order to obtain data to support the theory the author has carried out one of the most delightful pieces of research that could be imagined. Trips were made to the far corners of the world to study primitive tribes and races. The Swiss in isolated mountain valleys, the Gaels of the Hebrides islands, the Eskimo of coastal and interior Alaska, tribes of Central Africa and the waters of the Upper Nile, the Maori of New Zealand and aboriginal Australian tribes, the Melanasians and Polynesians of the South Sea Islands, the Indians of Peru and tribes of the headwaters of the Amazon were among those included in Dr. Price's studies. The author attempted to study groups little influenced by white civilization, and groups of the same tribes or races who had come under the influence of the white man's diet. Regardless of latitude or elevation, whether the primitive people were coastal, living on sea foods, or were agrarian, living far inland, the primitive peoples showed a negligible amount of dental caries and dental arch deformities when isolated from the diet of the white man. Studies of the same tribes or races showed a progressive increase in tooth decay the more intimately they became associated with and dependent upon the white man and store food—sugar, white flour and milled grains, and canned foods. Dr. Price's figures are too consistent to be a matter of chance. In addition to the dental studies, chemical and biologic analyses of the diets of the primitive tribes were made. Regardless of whether the diet of the primitive groups was built on the basis of sea foods or dairy products, certain definite differences were found when contrasted with the average diet of civilized races. The diets of the primitive races contained much larger quantities of calcium, phosphorus, magnesium, iron, and fat-soluble vitamins. It is Dr. Price's contention that it is a deficiency of these in the average modern civilized diet which leads to dental caries, which in turn is an expression of physical degeneration of civilized man. The descriptions of the food habits and sources of vitamins of some of the primitive groups is most interesting. The author feels we have much to learn from primitive diets and food habits. All of this lies in the realm of ascertained facts and to this extent the study is factually important.

From a strictly scientific viewpoint it would have been better had the author stopped at this point. However he drives on in a most interesting way to certain speculative ideas or hypotheses which are exceedingly stimulating but for which he has little factual data. When he steps out of his field into that of immunology, criminology, and abnormal mental development some of his ideas and deductions are quite open to question, as for example the relationship of bacterial immunity to diet. Implications that intelligence, delinquency, character and morals are in large part dependent upon diet, rather than upon heredity and environment, are not supported by the data in the book nor the author's studies. The difference is not as obvious to the lay reader as to one accustomed to scientific literatures. These theoretical deductions, however, are most interesting and when properly differentiated are important. Incidentally the book is a Scientific Book of the Month Club selection.

Report of Committee on Immunization of the American Academy of Pediatrics. Published by the American Academy of Pediatrics, Evanston, Ill. Price 10c.

This second edition of the Report has been decidedly increased in size and scope and, as a result, is very much improved over the first edition. For this reason it is even more valuable for the practitioner's desk than the first edition.

Correction

An error appears on page 10 of the "Report of the Committee on Immunization and Therapeutic Procedures for Acute Infectious Diseases of the American Academy of Pediatrics," which was recently sent to each member of the Academy. This error concerns the doses recommended for active immunization against scarlet fever. The sentence reads "A Dick-positive reactor may be rendered negative by injecting increasing skin test doses of scarlet fever toxin—500, 800, 2,000, 8,000 and 80,000 units at weekly intervals." This latter part should read "500, 2,000, 8,000, 25,000 and 80,000 units at weekly intervals."